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Original Communications

THE THERAPEUTIC VALUE OF A NEW CONCENTRATED STREPTOCOCCUS ANTITOXIN IN PUERPERAL FEVER*

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THE name, puerperal fever was first suggested by Richard Morton in 1692 to apply to a febrile condition in puerperal woman. Although the term is not precise and as vague as the knowledge of the condition was at the time it was first used, yet it has been retained to this day. It included a vast number of clinical entities giving fever during the puerperium, some of which are entirely unrelated to childbirth, such as pneumonia.

In this study puerperal fever will be considered as an acute infection of the female generative tract producing an acute inflammation of the uterus and its surrounding structures. The fact that various bacteria may be the cause of different pathologic and clinical pictures has not altered the nomenclature. Inasmuch as the term has reached such general acceptance, it will be used here also, with additional descriptive terms to specify the causative organism and the predominant pathologic picture. In the strict sense the term, puerperal fever, should be applied to an acute febrile condition occurring early in the puerperium with the pathologic picture of acute endometritis, which usually becomes associated with myometritis, salpingitis, parametritis, pelvic peritonitis and pelvic thrombophlebitis and may lead to generalized peritonitis, septicemia, septicopyemia or pelvic abscess. Principally, that type of puerperal fever due to the streptococcus will be considered in the following report.

*Read at a meeting of the Chicago Gynecological Society, May 18, 1928.

That the streptococcus is responsible for the majority of the severe puerperal infections has been known since Mayrhofer, in 1865, found the organism in smears from the tissues and Pasteur, in 1878, cultivated it from fatal cases. Further evidence of the etiology has been presented from time to time by the occurrence of puerperal fever in maternity hospitals in epidemics which were traced to a streptococcus infection. By analogy with other known streptococcal infections, such as scarlet fever and erysipelas one would logically expect advances in specific therapy. Up to the present time these have not occurred, and as a matter of fact the treatment of puerperal fever has not decreased its mortality.

The history of serum therapy in puerperal fever has been well related by Bailey in 1924, and therefore requires no detailed repetition. Only a brief summary with some additions will be given. In 1895 Marmorek produced the first streptococcus polyvalent serum. Other investigators (VandeVelde, Aronson, Neufeld and Rimpau, Meyer and Ruppeld, and Bar and Tissier) used polyvalent serums but the results were not encouraging. Meyer thought that he prepared a serum of antitoxic as well as bactericidal powers when he immunized an animal with a mixture of streptococci and their specific bactericidal serum. He assumed that the streptococci were dissolved in the serum thereby liberating endotoxins. However, Aronson disagreed with this assumption, since he demonstrated that the streptococcus could not be dissolved by body fluids, as could typhoid or cholera bacillus, but is rendered innocuous solely by phagocytosis. This impression is confirmed by the observation made in one of the cases (M. S.) reported below in which a viable streptococcus hemolyticus was cultivated from a tubo-ovarian abscess months after the infection.

According to Bailey, Park in 1909 utilized a number of strains of streptococci recovered from women dying of puerperal fever. The serum from the one horse injected was used for several years. Upon the death of this animal the work was discontinued. As no decided clinical evidence of the therapeutic value of the serum was published and as no bacteriologic diagnosis of the cases had been made, this work is of little or no significance.

Krongold-Vinover in 1921 infected horses with streptococci obtained from human sources and procured the serum fourteen or fifteen days later. A prophylactic injection of 0.1 c.c. of this serum into a mouse twenty-four hours before infection protected the animal against a dose of streptococci representing one hundred times the lethal dose. He introduced into puerperal fever patients on the first day, 20 c.c. of the serum with 180 c.c. of saline solution intravenously, on the second day 30 c.c. of serum with 270 c.c. of saline, and on the third day 40 c.c. of serum with 360 c.c. of saline. He reported 38 patients cured, in a series of 41 who showed streptococci in the cervix, and 2 out of 5 who had streptococci in the blood.

Zangemeister and Meissl employed human convalescent serum with good results. However, the obtaining of human sera for therapeutic purposes is difficult. Besides, Aronson and Heyneman were unable to show experimentally any advantage of the human sera over that of the horse.

Bailey (1924) used large doses (100 c.c. or more) of unconcentrated serum from a horse immunized with a mixture of strains which included the majority of hemolytic streptococci not only according to the serologic classification but also from the disease sources. In a series of 13 cases, there was a mortality of 15.3

per cent. From the history abstracts there was not in all cases evidence that the infection was in the uterus or due to the streptococcus.

From the report of a committee of the North of England Section at the fifth British Congress of Obstetrics and Gynecology of April, 1925, 104 cases were treated with serum combined with or without other operative procedures, with a mortality of 72 per cent while in 47 cases treated with serum alone the mortality was 76.5 per cent.

An attempt to determine the present status of antistreptococcus serum therapy in this country was made by E. Novak in 1926. The analysis of the questionnaires indicated that little reliance was placed on the commercial antistreptococcus serum.

Following our reports (Lash and Kaplan) of toxin production by the hemolytic streptococcus isolated from the blood of women with puerperal fever, and antitoxin production in rabbits, there appeared a report from Germany (Warnekros, et al) of the use of an antitoxic serum in the surprisingly large number of 200 women with severe puerperal fever, with the astounding result of no mortality. There was no evidence presented as to the causative bacteria or the stage of the infection.

The latest report of a streptococcus antitoxin used in puerperal fever is that of Gaessler's coming from the same clinic as the preceding one. In 341 obstetrical cases and 59 abortions, the serum was injected intragluteally in doses of 50 c.c. which were usually repeated daily until a fall in temperature occurred. There were 20 deaths, but of these only 3 were considered attributable to failure of the method.

In June of 1925 we (Lash and Kaplan) reported the production of toxin by hemolytic streptococci isolated from the blood of women with puerperal fever; later, we succeeded in preparing an antitoxic serum in rabbits. Efforts were then made to produce sufficient antitoxic serum in larger animals, such as sheep and then goats. It was soon found that sheep serum was toxic to humans as determined by intracutaneous injections, and that goats were unable to furnish sufficient serum for an extensive clinical study. With the cooperation of Dr. M. M. Powell and Mr. W. A. Jamieson, director of the biologic laboratories of Eli Lilly and Company, the above obstacles were overcome by immunizing horses.

One of the horses was immunized with increasing doses of toxin while the other was immunized with both toxin and organisms. Twelve strains of Streptococcus hemolyticus were used. These were isolated from women with puerperal fever and were determined to be toxin producers. The serum obtained neutralized the toxin of these strains as shown by cutaneous tests (Dick method). As yet, there is no evidence of a specific streptococcus for puerperal fever. However, it is logical to assume that bacteria, like all living matter, are probably altered by their environment and that streptococci isolated from infected puerperal uteri and the circulating blood may have a greater degree of

specificity in producing an antitoxic serum for puerperal fever than those found in other infections. This is only a working hypothesis.

In time, it was found that the serum obtained from the horse immunized with the toxin and streptococci had a higher antitoxin potency than that secured from the horse immunized with the toxin alone. This observation confirmed our earlier experimental studies (Lash and Kaplan).[9]

In addition to specificity and potency another desirable feature to be attained in serum preparation is the elimination of the frequent and severe serum reactions which occur when large doses of unconcentrated serum are used. The first cases treated with unconcentrated serum suffered from reactions which were avoided when the serum was concentrated.

In the following study the presence of a fever in a puerperal woman was not in itself sufficient reason for administration of serum, as it is not an uncommon occurrence for a puerperal woman to have a temporary fever with no other symptoms to establish its etiology. Only patients with definite evidence of infection in the uterus and pelvic tissues, such as pain and tenderness over the corpus with or without parametrial tenderness, together with fever and leucocytosis, were treated with serum. All stages of infection were treated as the purpose of this study was to evaluate, if possible, the new antitoxic streptococcus serum in puerperal fever in its various pathologic states.

Fifty-seven women in various stages of puerperal fever were given serum-therapy. The difficulty of separating accurately the various anatomicopathologic stages in puerperal fever during life is obvious. However, the fact that clinically one stage usually predominates, permits a classification which is of value for practical purposes. Of the cases treated, there were 20 of uncomplicated acute endometritis and metritis, 20 of acute endometritis and parametritis, 10 of pelvic peritonitis and generalized peritonitis, 3 of parametritis and thrombophlebitis, 4 of embolic pulmonary complications, and 2 of extrapelvic pathology simulating puerperal fever. This classification based on the predominating lesion is followed in Tables I to VI which contain a brief abstract of each case. Table VII contains a group of puerperal fever patients who did not receive any of the antitoxin.

In the administration of the puerperal fever antitoxin the usual precautions of serum-therapy must be observed. If a history of previous hypersensitiveness to serum is present, desensitization should be carried out. As to the route of injection, the intravenous one is preferred for rapidity of effect, but carries a greater risk of reaction than the intramuscular method. The dose of the serum has been very appreciably decreased since it has been concentrated. Thus early in the work, 100 to 200 c.c. of the serum were given and immediate reactions oc-

TABLE I. ACUTE ENDOMETRITIS

PATIENT	CHARACTER OF DELIVERY	ONSET OF PUERPERAL FEVER	CLINICOPATHOLOGIC DIAGNOSIS	T.P.R. DAY P.P.	BLOOD COUNT	BACTERIOLOGY CERVIX	SERUM-THERAPY PUERPERAL FEVER ANTITOXIN	RESULT AND COMMENT
A. S. C. 24 P. I	Precipitate labor (15 min.)	Fifth day fever	Acute endometritis	Sixth day 102^{6}- 120 -24	11,500	G-Bacilli. Streptococci on smear	Sixth day P.P.* 100 c.c. of unconcentrated P.F.A.** intravenously. Chill, serum reaction	Afebrile four days after serum. Home ten days. i.e., seventeen days P.P.
A. R. W. 46 P. XIV	Prolapsed pulseless cord Craniotomy Uterus packed	Third day fever	Acute endometritis	Fifth day 102^{6}- 100 -24	4,400	Streptococcus non-hemolyticus	Fifth day P.P. 40 c.c. of concentrated P.F.A. intravenously	Home fourteenth day P.P. Afebrile seventh day P.P. followed by moderate rises eighth and ninth days
F. M. C. 19 P. I	Eclampsia low forceps. Episiotomy with repair	Sixth day fever Headache	Acute endometritis	Tenth day 102^{4}- 120 -22	26,300	Streptococcus hemolyticus	Tenth day P.P. 20 c.c. of conc. P.F.A. intravenously	Afebrile eleventh day P.P. Home thirteenth day release
M. Z. W. 39 P. IV	Incomplete abortion. Curettage. Uterine pack	Fifth day fever	Acute endometritis	Sixth day 102 - 120 -22	Not made	Streptococcus non-hemolyticus	Sixth day P.P. 40 c.c. of conc. P.F.A. intravenously	Afebrile seventh day P.P. Rise to 100° on ninth day P.P. only. Home twentieth day P.P.
O. D. C. 17 G. II	Spontaneous abortion	Third day severe pain in lower abdomen chill and fever	Acute endometritis Parametritis	Sixth day 103^{2}- 112 -26	24,500	Streptococcus in broth outgrown on plate	Sixth day P.P. 40 c.c. of conc. P.F.A. intrav. Seventh day P.P. 40 c.c. of conc. P.F.A. intramuscularly	General condition good; septic course through fourteenth day P.P. Home twenty-first day P.P.

Note: In order to conserve space abbreviations are used where possible as:
*P.P. Postpartum.
**P.F.A. Puerperal fever antitoxin.
The same will hold for the other tables.
Blood cultures positive in only two patients (E. W. and M. D.).

TABLE I—CONT'D

PATIENT	CHARACTER OF DELIVERY	ONSET OF PUERPERAL FEVER	CLINICOPATHOLOGIC DIAGNOSIS	T.P.R. DAY P.P.	BLOOD COUNT	BACTERIOLOGY CERVIX	SERUM-THERAPY PUERPERAL FEVER ANTITOXIN	RESULT AND COMMENT
B. B. C. 21 P. I	Preeclampsia Spontaneous	Third day fever Abdominal pains, vomited	Acute endometritis	Third day 104^{6}- 132 -24	17,100	Strept. nonhem.	Third day P.P. 100 c.c. of goat serum intraven. Serum reaction vomited. Fourth day P.P. 40 c.c. of conc. P.F.A. intravenously	Afebrile seventh day P.P. Occasional fever. Home eighteenth day.
A. D. W. 18 P. I	Fundal cesarean section; labor, 24 hours	Second day fever	Acute endometritis Peritonitis	Fourth day 101^{8}- 88 -22	14,500	Smears. Streptococci bacilli	Fourth day P.P. 40 c.c. of conc. P.F.A. intravenously	Afebrile twelfth day P.P. Home twentieth day P.P.
J. C. C. 18 P. I	Low forceps. Preeclampsia	Second day fever	Acute endometritis	Third day 101^{8}- 140 -24	15,050	Strept. nonhem.	Third day P.P. 100 c.c. goat serum intrav. Fourth day P.P. 60 c.c. conc. P.F.A. intramuscularly	Afebrile eleventh day P.P. Home fourteenth day P.P.
B. H. W. 31 P. II	Labor 48 hours Classical cesarean section	First day fever and chill, headache	Acute endometritis Peritonitis	Fourth day 103^{4}- 132 -36	21,700	Streptococcus on smear	Fourth day P.P. 40 c.c. P.F.A. intraven. Fifth day P.P. 20 c.c. P.F.A. intramus. Sixth day P.P. 20 c.c. P.F.A. intramus.	Afebrile tenth day P.P. Home fifteenth day P.P.
M. P. C. 26 P. IV	Spontaneous easy	Third day fever, severe pain in abdomen, headache	Acute endometritis	Fifth day 103 - 124 -24	19,000	Anaerobic. Strept. nonhem.	Fifth day P.P. 20 c.c. P.F.A. intraven., 20 c.c. P.F.A. intramus. Sixth day P.P. 40 c.c. P.F.A. intraven., 20 c.c. P.F.A. intramus. Seventh day P.P. 20 c.c. P.F.A. intramus.	Afebrile ninth day P.P. Home twelfth day P.P.

TABLE I—CONT'D

PATIENT	CHARACTER OF DELIVERY	ONSET OF PUERPERAL FEVER	CLINICOPATHOLOGIC DIAGNOSIS	T.P.R. DAY P.P.	BLOOD COUNT	BACTERIOLOGY CERVIX	SERUM-THERAPY PUERPERAL FEVER ANTITOXIN	RESULT AND COMMENT
J. J. C. 20 P. I	Labor induced by cervical pack, labor 24 hr. Low cervical cesarean. B.O.W. rupt. ten hours	Second day fever	Acute endometritis Peritonitis	Fourth day 105^{4} 124 -44	6,000 Next day 12,900	Strept. non-hem.	Fourth day P.P. 20 c.c. P.F.A. intrav., 20 c.c. P.F.A. intramus. Fifth day P.P. 40 c.c. P.F.A. intramus. Sixth day P.P. 40 c.c. P.F.A. intramus. Seventh day P.P. 20 c.c. P.F.A. intramus. Serum reaction. (Urticaria.) Tenth day P.P.	Afebrile ninth day P.P. Home fifteenth day P.P.
F. O. C. 25 P. II	Induced abortion, catheter	First day chills, fever and sweats Pain in lower abdomen	Acute endometritis Peritonitis	Eighth day 105^{6} 116 -22	10,600	Strept. non-hem. Staph. albus. hem.	Eighth day P.P. 40 c.c. P.F.A. intrav., 20 c.c. P.F.A. intramus. Ninth day P.P. above repeated. Tenth and eleventh days P.P. 20 c.c. P.F.A. intramus.	Afebrile twenty-fifth day P.P. Home thirty-seventh day P.P.
C. J. C. 18 P. I	Low forceps Episiotomy	Second day fever	Acute endometritis	Fifth day 102^{6} 104 -24	14,500	Strept. non-hem. Staph. albus. hem. B. coli.	Fifth day P.P. 40 c.c. P.F.A. intramus. Sixth day P.P. 20 c.c. P.F.A. intramus.	Afebrile seventh day P.P. Home thirteenth day P.P.
T. W. W. 28 P. IV	Spontaneous abortion	Second day fever	Acute endometritis	Fourth day 104 - 104 -24	5,950	Strept. non-hem. Staph. albus.	Fourth day P.P. 40 c.c. P.F.A. intraven.	Afebrile fifth day P.P. Home twelfth day P.P.

TABLE I—CONT'D

PATIENT	CHARACTER OF DELIVERY	ONSET OF PUERPERAL FEVER	CLINICOPATHOLOGIC DIAGNOSIS	T.P.R. DAY P.P.	BLOOD COUNT	BACTERIOLOGY CERVIX	SERUM-THERAPY PUERPERAL FEVER ANTITOXIN	RESULT AND COMMENT
F. G. C. 21 P. I	Bicornuate uterus. Transverse cervical cesarean. B.O.W. rupt. 10 hours	First day fever	Gonorrheal, endocervicitis Acute endometritis	Fourth day 103^{2}- 144 -28	14,700	Smear. Strept. Staph. Gonococci.	Fourth day P.P. 20 c.c. P.F.A. intrav., 20 c.c. P.F.A. intramus.	Afebrile eighth day P.P. Pulse 100. Home thirty-fifth day P.P.
C. R. W. 20 P. I.	Self-induced abortion. Douche-tip	First day fever, pain in lower abdomen	Acute endometritis	First day 105 - 148 -30	28,450	Not taken	First day P.P. 20 c.c. P.F.A. intrav., 20 c.c. P.F.A. intramus.	Afebrile second day P.P. Home eighth day P.P.
G. W. C. 15 P. I	Labor 33½ hr. High forceps Cervical and perineal lacerations, second degree	Second day fever, abdominal pain	Acute endometritis Peritonitis	Sixth day 105^{6}- 160 -30	22,950	Strept. nonhem.	Sixth day P.P. 20 c.c. P.F.A. intraven.	Afebrile seventh day P.P. with occasional rise to 100. Home thirtieth day P.P.
E. W. W. 22 P. III	Labor 50 hours Spontaneous Home by M.D.	Second day Severe chills, fever	Acute endometritis, peritonitis, septicemia	Fourth day 102^{2}- 144 -28	16,750	Strept. nonhem. Strept. nonhem. in blood	Fourth day P.P. 40 c.c. P.F.A. intravenously	Death 2½ hr. later. Serum death? Autopsy. Acute metritis. Salpingo-oophoritis. Pelvic peritonitis

TABLE I—CONT'D

PATIENT	CHARACTER OF DELIVERY	ONSET OF PUERPERAL FEVER	CLINICOPATHOLOGIC DIAGNOSIS	T.P.R. DAY P.P.	BLOOD COUNT	BACTERIOLOGY CERVIX	SERUM-THERAPY PUERPERAL FEVER ANTITOXIN	RESULT AND COMMENT
M. D. C. 21 P. V	Spontaneous (Home by M.D.)	Fifth day fever	Acute endometritis Beginning parametritis Thrombophlebitis	Seventh day 104-132 -22	14,200	Strept. in broth. Overgrown on plate by contam. Strept. hem. in cervix	Seventh day P.P. 40 c.c. P.F.A. intramus. Eighth day P.P. 20 c.c. P.F.A. intramus. Serum reaction. Twenty-second day P.P.	Temporary thrombophlebitis right arm on twelfth day P.P. Afebrile eighteenth day P.P. Home twenty-eighth day P.P.
A. E. C. 27 P. V	Spontaneous	Second day fever	Acute endometritis	Sixth day 104-116 -24	13,306	Strept. hem.	Sixth day P.P. 40 c.c. P.F.A. intraven. Vomited 5 min. later. Serum reaction. Tenth day P.P.	Afebrile ninth day P.P. Home sixteenth day P.P.

TABLE II. ACUTE ENDOMETRITIS, PARAMETRITIS

PATIENT	CHARACTER OF DELIVERY	ONSET OF PUERPERAL FEVER	CLINICOPATHOLOGIC DIAGNOSIS	T.P.R. DAY P.P.	BLOOD COUNT	BACTERIOLOGY CERVIX	SERUM-THERAPY	RESULT AND COMMENT
C. K. W. 19 P. I	Self-induced abortion (catheter)	Fifth day, chills, and fever	Acute endometritis, parametritis, peritonitis, septicemia	102 - 148 -60 Twenty sixth day	25,400	Streptococcus hemolyticus	Twenty-sixth day 50 c.c. of goat serum intraven. Twenty-eighth day 85 c.c. of goat serum intraven.	Death thirtieth day. Late case
R. D. C. 20 P. II	Spontaneous, easy (home by out-patient disp.)	Second day, pain in lower abdomen Fever and vaginal bleeding	Acute endometritis, parametritis, pelvic peritonitis, thrombophlebitis	104^{8}-108 -24 Fifth day	15,750	Streptococcus hemolyticus	Ninth and eleventh days 100 c.c. of goat serum intraven. Reaction, chill, back-pain	Recovery, left pelvic mass. Swelling in left leg subsided. Home twenty-ninth day
M. A. W. 24 P. I	Spontaneous, easy (home by doctor)	Fifth day fever	Acute endometritis, parametritis, pelvic peritonitis	103^{4}-104 -26 Seventh day	16,800	Streptococcus hemolyticus	Seventh and fifteenth days 20 c.c. P.F.A. intravenously	Released thirty-fourth day. Septic course, no complaints. Pelvic pathology
B. P. W. 23 P. I	15 hr. and 10 min. Low forceps Cervical laceration Episiotomy Preeclampsia	Seventh day fever B.P. 176-80	Preeclamptic toxemia Hypertension and album. Acute endometritis, parametritis and pelvic peritonitis Anemia	102^{6}-152 -30 Fourteenth day	26,300	Streptococcus hemolyticus	Fourteenth day 100 c.c. goat serum intravenously	Death fifteenth day, eighteen hours after serum injection. Toxemia and anemia

TABLE II—CONT'D

PATIENT	CHARACTER OF DELIVERY	ONSET OF PUERPERAL FEVER	CLINICOPATHOLOGIC DIAGNOSIS	T.P.R. DAY P.P.	BLOOD COUNT	BACTERIOLOGY CERVIX	SERUM-THERAPY	RESULT AND COMMENT
L. J. W. 37 P. V	Self-induced abortion. (Slippery elm Ergoapiol Capsules)	Second day Pain in lower abdomen, chills, fever and vomiting	Acute endometritis, parametritis, and pelvic peritonitis	101^{6}-140 -32 Eighth day	19,900	Not taken	Eighth day P.F.A. 40 c.c. intraven. Ninth day repeated above. Eleventh, twelfth, thirteenth and fourteenth days 20 c.c. P.F.A. intramuscularly	Recovery afebrile after fifteenth day, pelvic path.
E. H. C. 22 P. I	Labor 78 hr. Dührssen's incisions, midforceps P.P. Hem. No cervical repair	Intrapartum and third day chill, fever, pain in lower abdomen	Acute endometritis, parametritis, finally localizing on right side	104^{4}-120 -20 Tenth day	19,400	Strept. hemolyticus. B. coli.	Tenth day 40 c.c. P.F.A. intramus. Twelfth day 40 c.c. intraven. Thirteenth day 40 c.c. P.F.A. intramus. Fourteenth day 20 c.c. intramus. Eighteenth day 20 c.c. intramus. Twentieth day 40 c.c. intramus.	Released twenty-fourth day. Feels fine. Right parametritis, P.M. fever
F. M. W. 37 P. II	Self-induced abortion	Seventh day Chills and fever, pain in lower abdomen	Acute endometritis, parametritis, pelvic peritonitis, becoming generalized	103^{4}-120 -26 Tenth day	19,200	B. coli. Streptococcus nonhemolyticus	Tenth day P.P. 20 c.c. P.F.A. intraven. Eleventh day 20 c.c. P.F.A. intramus. Twelfth day P.P. 40 c.c. P.F.A. intraven. Fifteenth day P.P. 20 c.c. P.F.A. intramuscularly	Septic course with bleeding. Curettage for bleeding. Twenty-first day P.P. Left parametritis. Twenty-seventh day P.P. afebrile. Psycho. hosp. Dementia precox

TABLE II—CONT'D

PATIENT	CHARACTER OF DELIVERY	ONSET OF PUERPERAL FEVER	CLINICOPATHOLOGIC DIAGNOSIS	T.P.R. DAY P.P.	BLOOD COUNT	BACTERIOLOGY CERVIX	SERUM-THERAPY	RESULT AND COMMENT
M. S. C. 18 P. I	Self-induced abortion Pencil into vagina or cervix?	Seventh day Severe pain in lower abdomen Nausea and vomiting, chills and fever	Acute endometritis, parametritis, pelvic peritonitis, becoming generalized	101 - 124 -22 Fifteenth day	25,100	No growth	Fifteenth day P.P. 40 c.c. P.F.A. intrav., 40 c.c. intramus. Seventeenth day P.P. 20 c.c. P.F.A. intramus. Twenty-first day P.P. 20 c.c. P.F.A. intramus.	Home twenty-ninth day P.P. Returned, operated ten weeks later. Right tubo-ovarian abscess, left salpingitis, pus-streptococcus hemolyticus
L. M. W. 18 P. I	Spontaneous easy (home by M.D.) B.O.W. rupt. by doctor	Second day, fever, chills, vomiting, soreness in lower abdomen	Acute endometritis, parametritis, pelvic peritonitis	103 - 130 -28 Fifth day	6,600	Streptococcus non-hemolyticus	Fifth day P.P. 40 c.c. P.F.A. intraven. Sixth day P.P. 40 c.c. P.F.A. intrav., 20 c.c. P.F.A. intramus. Seventh day 40 c.c. P.F.A. intramus. Eighth day 20 c.c. P.F.A. intramus. Eleventh day P.P. serum reaction	Home. Afebrile from sixteenth day P.P.
D. M. C. 23 P. I	Classic cesarean section Labor 19 ½ hr.	Second day fever	Acute endometritis, parametritis, pelvic abscess, pelvic peritonitis	1048- 100 -22 Second day	20,500 15th day	Strept. on smear. B. coli cultured	Prophylactic 20 c.c. P.F.A. intramus. after operation. Second day P.P. 20 c.c. P.F.A. intramuscularly	High temp. and pulse unchanged. Sixteenth day P.P. post colpotomy. Home fifty-eighth day P.P.
O. F. C. 22 P. I	Induced abortion (curettage three times)	Seventh day, fever, chills, bleeding	Acute endometritis, parametritis, extending pelvic peritonitis	1034- 120 -20 Eleventh day P.P.	17,850	Streptococcus hemolyticus. Staphylococcus hemolyticus	Eleventh day P.P. 40 c.c. P.F.A. intravenously	Home thirty-first day P.P. Afebrile from thirteenth day.

TABLE II—CONT'D

PATIENT	CHARACTER OF DELIVERY	ONSET OF PUERPERAL FEVER	CLINICOPATHOLOGIC DIAGNOSIS	T.P.R. DAY P.P.	BLOOD COUNT	BACTERIOLOGY CERVIX	SERUM-THERAPY	RESULT AND COMMENT
M. L. C. 42 P. XIV	Bag induction Labor 36 hr. Purulent amniotic fluid	Intrapartum	Acute endometritis, parametritis, peritonitis, septicemia	103 - 130 -20 Ninth day P.P.	17,950	B. coli. Streptococcus nonhem. Streptococcus hemolyticus and anaerobic in blood	Ninth day P.P. 20 c.c. P.F.A. intrav. Tenth day P.P. 20 c.c. P.F.A. intrav., 20 c.c. P.F.A. intramus. Eleventh day 20 cc. P.F.A. intramus. Thirteenth day 20 c.c. P.F.A. intramus. Fifteenth day P.P. P.F.A. intramus. Twenty-first day P.P. P.F.A. intramuscularly.	Released twenty-fourth day P.P. Mild septic course
E. E. C. 23 P. II	Spontaneous abortion	Seventh day, chill and fever	Acute endometritis, parametritis, septic bronchopneumonia, septicemia	103+- 116 -24 Eighth day P.P.	18,200	Streptococcus nonhem.	Eighth day P.P. 40 c.c. P.F.A. intravenously. Twenty-sixth day P.P. x-ray, lung abscess right upper, left lower lobe, thirty-ninth day P.P. Tubercle bacilli in sputum. Resolving infarcts with M.A. pulmonary T.B.	Pulse down to 78, temperature 101°-103°
E. R. C. 30 P. VI	Spontaneous easy	Seventh day, bleeding, abdominal cramps, fever	Acute endometritis, parametritis, pelvic peritonitis	104+- 112 -36 Fourteenth day P.P.	18,400	Streptococcus nonhem. Staph. albus.	Fourteenth day P.P. 40 c.c. P.F.A. intramus.	Afebrile seventeenth day P.P. Occasional rise to 101°. Home. Seventeen days in hospital. Thirty-first day P.P.

TABLE II—CONT'D

PATIENT	CHARACTER OF DELIVERY	ONSET OF PUERPERAL FEVER	CLINICOPATHOLOGIC DIAGNOSIS	T.P.R. DAY P.P.	BLOOD COUNT	BACTERIOLOGY CERVIX	SERUM-THERAPY	RESULT AND COMMENT
B. O. C. 30 P. VI	Expulsion of hydatid mole malignant sore throat	First day fever	Acute endometritis, parametritis, chorioepithelioma, extension into parametrium with perforation into vagina	104^{8}-136 -28 Second day P.P.	15,750	Streptococcus nonhem. Staph. albus	Second day P.P. 40 c.c. P.F.A. intramus. Twelve days later serum reaction	Eighth day P.P. hemorrhage. 4200 mg. radium. Temp. continued high, pulse low, transferred to another hospital for x-ray therapy. Too many factors for analysis
D. W. C. 21 P. III	Induced abortion (midwife)	Second day fever	Acute endometritis, parametritis, pelvic peritonitis, septicemia	105^{5}-144 -36 Fourth day P.P.	10,150	B. coli. Staphylococcus albus. Few streptococcus nonhem.	Fourth day P.P. 40 c.c. P.F.A. intraven.	Septic course unabated. Died fifteenth day P.P. Coroner's autopsy, general septicemia
M. S. C. 24 P. III	Spontaneous abortion	First day P.P. chills, fever, vomited	Acute endometritis, parametritis, pelvic peritonitis, pyelitis	103^{4}-120 -28 Eighth day P.P.	28,200	No growth	Eighth day P.P. 40 c.c. P.F.A. intraven.	Released tenth day P.P. Septic course unabated
M. M. C. 19 P. I	Cervical cesarean	Second day P.O. Fever, pain in lower abdomen	Acute endometritis, parametritis, pelvic peritonitis, pyelitis	101 -126 -24 Seventh day P.P.	11,500	Vagina B. coli.	Seventh day P.P. 80 c.c. goat serum intraven.	Afebrile twenty-fourth day P.P. Home, well

TABLE II—CONT'D

PATIENT	CHARACTER OF DELIVERY	ONSET OF PUERPERAL FEVER	CLINICOPATHOLOGIC DIAGNOSIS	T.P.R. DAY P.P.	BLOOD COUNT	BACTERIOLOGY CERVIX	SERUM-THERAPY	RESULT AND COMMENT
A. P. W. 29 P. III	Induced abortion (medicine plus?)	First day P.P. bleeding from vagina Fever and chills Pain in lower abdomen	Acute endometritis, parametritis, septicemia	Thirty-fifth day P.P. 100^{6}-128 -28	18,800		Thirty-fifth day P.P. 20 c.c. P.F.A. intraven.	Death thirty-sixth day P.P. Cardiac dilatation. Coroner's autopsy, general sepsis
R. G. W. 26 P. I	Induced abortion (catheter)	Sixth day P.P. fever, chills, pain in lower abdomen	Acute endometritis, parametritis	Ninth day 105 - 140 -22	9,200 marked anemia		Ninth day P.P. 40 c.c. P.F.A. intraven.	Blood transfusion followed by chill, restlessness, air-hunger, poor pulse. Death 6 hr. later

TABLE III. ACUTE PERITONITIS

PATIENT	CHARACTER OF DELIVERY	ONSET OF PUERPERAL FEVER	CLINICOPATHOLOGIC DIAGNOSIS	T.P.R. DAY P.P.	BLOOD COUNT	BACTERIOLOGY CERVIX	SERUM-THERAPY PUERPERAL FEVER ANTITOXIN	RESULT AND COMMENT
P. D. W. 21 P. I	Induced abortion	First day pain in lower abdomen, vaginal bleeding	Acute metritis, generalized peritonitis, septicemia	Sixth day	8,400	Strept. hem. Strept. hem. in blood	Sixth day P.P. 20 c.c. P.F.A. intraven. Seventh day P.P. 20 c.c. P.F.A. intrav., 20 c.c. P.F.A. intramus.	Death eighth day P.P. Coroner's autopsy, traumatic perforated uterus, acute peritonitis
J. L W. 27 P. III	Spontaneous (home by midwife)	Third day pain in lower abdomen, chills and fever	Acute metritis, generalized peritonitis, right lower pleurisy	Ninth day 100^{8}-140 -56	11,100	Strept. nonhem.	Ninth day P.P. 110 c.c. goat serum, serum reaction	Death eleventh day P.P Coroner's autopsy, generalized peritonitis
E. S. W. 32 P. I	Induced abortion	First day pain in lower abdomen, vomited	Acute endometritis, generalized peritonitis	Fifth day 102^{6}-172?36	21,050	Anaerobic strept. nonhem.	Fifth day P.P. 50 c.c. P.F.A. intraven.	Death sixth day P.P. Coroner's autopsy, generalized purulent peritonitis
J. G. W. 39 P. IV	Spontaneous miscarriage, 6½ months	First day pain in lower abdomen, chills and fever, vomiting	Acute endometritis, generalized peritonitis	Sixth day 101^{8}-104 -24	13,550	Strept. hem.	Sixth day P.P. 40 c.c. P.F.A. intraven. Ninth day P.P. 40 c.c. P.F.A. intravenously	Death eleventh day P.P. Generalized peritonitis
G. G. C. 15 P. I	Spontaneous, perineal laceration, second degree	Third day pain in lower abdomen. Toxic	Acute parametritis, peritonitis	Eighth day 103 -132 -38	5,750	Strept. hem. postmortem strept. hem. in blood	Eighth day P.P. 40 c.c. P.F.A. intra. Ninth day P.P. 40 c.c. P.F.A. intramus. Tenth day P.P. 40 c.c. P.F.A. intramus. Eleventh day P.P. 20 c.c. P.F.A. intramus.	Death twelfth day P.P. Autopsy, generalized serous fibrinous peritonitis

Blood cultures positive in three patients. (P. D., G. G., B. G.)

TABLE III—CONT'D

PATIENT	CHARACTER OF DELIVERY	ONSET OF PUERPERAL FEVER	CLINICOPATHOLOGIC DIAGNOSIS	T.P.R. DAY P.P.	BLOOD COUNT	BACTERIOLOGY CERVIX	SERUM-THERAPY PUERPERAL FEVER ANTITOXIN	RESULT AND COMMENT
M. M. W. 42 P. X	Spontaneous, easy, P.P. hem. (home by midwife)	Third day P.P. pain in abdomen nausea and vomiting	Acute endometritis, generalized peritonitis	Fifth day 104- 160?-52	8,000	Streptococcus nonhem.	Fifth day P.P. 40 c.c. P.F.A. intraven.	Death sixth day P.P. Virulent generalized peritonitis. No autopsy
F. S. W. 22 P. III	Induced abortion (by M.D.)	First day P.P. severe pain in lower abdomen, vaginal bleeding, fever	Acute metritis, generalized peritonitis	Fourth day 103- 160 -36	25,400		Ninth day P.P. 40 c.c. P.F.A. intraven. Tenth day P.P. 20 c.c. P.F.A. intraven., 30 c.c. P.F.A. intramus.	Death eleventh day P.P. Coroner's autopsy, acute purulent peritonitis
B. H. C. 16 P. I	Spontaneous abortion followed by curettage (home by M.D.)	Fourth day P.P. pain in lower abdomen, fever	Acute metritis, parametritis, peritonitis, pneumonia	Fifteenth day 101- 120 -36	22,750	Strept. hem.	Fifteenth day P.P. 40 c.c. P.F.A. intraven., 20 c.c. P.F.A. intramus.	Death seventeenth day P.P. Coroner's autopsy, general sepsis
V. L. W. 33 P. I	Induced abortion (slippery elm) 12 previous induced abortions	Fifth day P.P. pain in lower abdomen, chills, and fever	Acute metritis, generalized peritonitis	Thirteenth day 101 - 138 -26	16,950	Strept. nonhem.	Thirteenth day P.P. 40 c.c. P.F.A. intramus. Fourteenth day P.P. 20 c.c. P.F.A. intramus.	Fever subsided for three days, then recurred for six days, then subsided. Home thirty-fifth day P.P.
B. G. C. 22 P. I	Spontaneous (home by midwife)	Fourth day P.P. pain in abdomen, distension, fever, slight nausea	Acute metritis, generalalized peritonitis	Ninth day 104- 160 -42	31,250	Strept. nonhem. Postmortem. Strept. nonhem. in blood	Ninth day P.P. 40 c.c. P.F.A. intraven. Tenth day P.P. 40 c.c. P.F.A. intramuscularly	Death eleventh day P.P. Autopsy, purulent phlebitis of uterus, diffuse fibro-purulent peritonitis

TABLE IV. ACUTE PARAMETRITIS, THROMBOPHLEBITIS

PATIENT	CHARACTER OF DELIVERY	ONSET OF PUERPERAL FEVER	CLINICOPATHOLOGIC DIAGNOSIS	T.P.R. DAY P.P.	BLOOD COUNT	BACTERIOLOGY CERVIX	SERUM-THERAPY PUERPERAL FEVER ANTITOXIN	RESULT AND COMMENT
A. B. W. 18 P. I	Classic cesarean section	Sixth day P.P. fever and chills	Acute endometritis, parametritis, peritonitis, thrombophlebitis of pelvic veins and left brachial vein	Twenty-sixth day 105^{4}- 146 -32	76,000	Strept. on smear, outgrown by B. coli. on plate	Twenty-sixth day P.P. uncon.* intrav. Twenty-eighth day P.P. 100 c.c. P.F.A. uncon. intrav.	Fever lower twenty-eighth to thirty-second day P.P. High fever from thirty-third to fifty-eighth day P.P Home seventieth day.
G. D. W. 23 P. I	Preeclampsia, low forceps, episiotomy	Second day P.P. fever, pain in lower abdomen	Acute endometritis, parametritis, pelvic thrombophlebitis	Third day 104^{2}- 124 -26	18,400	Strept. hem.	Third day P.P. 60 c.c. P.F.A. intramus. Fourth day P.P. 40 c.c. intramus. Twelfth day P.P. serum reaction. Seventeenth day P.P. desensitized, 40 c.c. P.F.A. intramus.	Afebrile sixth day P.P. Swelling left leg with tenderness along femoral vein, twenty-second day P.P. to twenty-sixth day P.P. Home thirty-seventh day P.P.
E. F. C. 32 P. II	Spontaneous abortion (?)	Second day P.P. chills, fever, vaginal bleeding	Acute endometritis, parametritis, pelvic thrombophlebitis, polyarthritis, septicemia	Fourth day 104^{2}- 124 -40	12,000		Fourth day P.P. 40 c.c. P.F.A. intramus.	Septic course unabated. Death eleventh day P.P. No autopsy

*Unconcentrated.

TABLE V. ACUTE PARAMETRITIS WITH PULMONARY COMPLICATIONS

PATIENT	CHARACTER OF DELIVERY	ONSET OF PUERPERAL FEVER	CLINICOPATHOLOGIC DIAGNOSIS	T.P.R. DAY P.P.	BLOOD COUNT	BACTERIOLOGY CERVIX	SERUM-THERAPY PUERPERAL FEVER ANTITOXIN	RESULT AND COMMENT
I. D. W. 38 P. V	Spontaneous abortion, manual removal of placenta Prolapsus uteri	Second day P.P. fever	Acute endometritis, parametritis, pulmonary embolus, infaret with abscess	Fourth day 103^{6}- 116 -26	17,500	Strept. nonhem. Spirilli on smear sputum, pneumococci.	Fourth day P.P. 20 c.c. P.F.A. intramus. Thirteenth day P.P. 20 c.c. P.F.A. intrav., 20 c.c. P.F.A. intramus.	Septic course unchecked until fourteenth day. Home thirty-second day P.P.
M. J. C. 16 P. I	Bag induction Prolapsed cord Episiotomy	First day P.P. pain in lower abdomen, fever, chill on third day	Acute endometritis, parametritis, pulmonary embolus, infaret with abscess and empyema	Third day 103^{2}- 140 -24	20,750	Strept. nonhem. Spirilli and B. fusiformis on smear	Third day P.P. 40 c.c. P.F.A. intrav., 20 c.c. P.F.A. intramus.	Fourth day P.P. general condition improved. Sudden pain in right side of chest. Infaret present. X-ray empyema. Thoracotomy with needle. 75 c.c. foul, grayish-green pus. Strept. nonhem. in culture. Home forty-second day P.P.
L. B. C. 20 P. I	Spontaneous, labor 50 hr., 20 minutes	Fifth day . P.P. Fever, pain lower abdomen	Acute endometritis, parametritis, septic embolus, marked infarction. (After rectal examination)	Eleventh day 101^{6}- 132 -24	16,400	Strept. nonhem. B. coli.	Eleventh day P.P. 40 c.c. P.F.A. intraven.	Death thirteenth day P.P. Septicemia, pulmonary infarction. No autopsy
J. M. C. 38 P. IV	Miscarriage 5 months Manual removal of placenta	First day P.P. Fever, pain in lower abdomen	Acute gangrenous endometritis, parametritis, bronchopneumonia	Third day 103 - 132 -32	22,000	Strept. nonhem.	Third day P.P. 20 c.c. P.F.A. intrav., 20 c.c. P.F.A. intramus.	Death tenth day P.P. Autopsy, ulcerative gangrenous metritis, purulent parametritis. Multiple septic infarcts of both lungs and multiple acute abscess of both lungs.

TABLE VI. EXTRAPELVIC PUERPERAL CONDITION

PATIENT	CHARACTER OF DELIVERY	ONSET OF PUERPERAL FEVER	CLINICOPATHOLOGIC DIAGNOSIS	T.P.R. DAY P.P.	BLOOD COUNT	BACTERIOLOGY CERVIX	SERUM-THERAPY PUERPERAL FEVER ANTITOXIN	RESULT AND COMMENT
A. T. C. 24 P. I	Spontaneous, (home by M.D.)	Third day P.P. abdominal pains, fever	Acute endometritis. Probable generalized miliary tuberculosis	Eighteenth 102 - 128 -28	4,600	Strept. viridans	Eighteenth day P.P. 100 c.c. goat serum intravenously	Septic course unchanged. Released twentieth day P.P. Died twenty-third day P.P. at home. No autopsy.
A. F. W. 36 P. III	Self-induced abortion 2½ months	First day P.P. chills, fever, pains in chest and abdomen	Acute endometritis, septic bronchopneumonia, septicemia	Third day 1044- 120 -40	38,800	Pneumococci	Third day P.P. 40 c.c. P.F.A. intraven. Fourth day P.P. 40 c.c. P.F.A. intramus.	Death seventh day P.P. Coroner's autopsy, right lobar pneumonia

TABLE VII. CONTROLS

PATIENT	CHARACTER OF DELIVERY	ONSET OF PUERPERAL FEVER	CLINICOPATHOLOGIC DIAGNOSIS	T.P.R. DAY P.P.	BLOOD COUNT	BACTERIOLOGY CERVIX	GENERAL THERAPY NO ANTITOXIC SERUM	RESULT AND COMMENT
G. M. C. 22 P. I	Version and extraction	First day P.P. Pain in lower abdomen Fever	Acute endometritis, metritis, septicemia, healing ischiorectol abscess, opened 13 days before delivery	First day 102^{6}- 120 -28	28,000	Strept. viridans Pneumococci	Sixth day P.P. 30 c.c., 1% mercurochrome intravenously. Eighth day P.P. repeated. Tenth day P.P. repeated.	Some improvement after third injection. Arthritis of left elbow and cutaneous abscess in right buttock. Both yielded Strept. hem. Recovery—91 days in hospital. Ankylosis of left elbow
P. H. C. 24 P. IV	Waiting mother in hospital Spont. 2 hr. labor	Second day P.P. Fever, abdominal pain, emesis	Acute endometritis, metritis, septicemia	Second day 101^{6}- 120 -24	4,200	Strept. hem. also in blood	Second day P.P. 30 c.c., 1% gentian violet intravenously	Died on the sixth day P.P.
H. B. W. 23 P. II	Spontaneous at home (by M.D.)	First day P.P. Fever	Acute endometritis, metritis, beginning peritonitis, septicemia	Fifth day 104 - 142 -48	22,500	Strept. hem.	Fourth day P.P. 20 c.c. commercial antistrept. serum given by doctor at home.	Died on the seventh day P.P. Autopsy, generalized serofibrinopurulent peritonitis. Focal bronchopneumonia and focal necrosis of liver
M. B. C. 28 P. VIII	Spontaneous abortion 3 mon. at home	First day P.P. Pain in lower abdomen, slight vaginal bleeding	Acute endometritis, metritis, beginning peritonitis	First day 100 - 110 -22		Strept. nonhem.	General measures	Died on fifth day P.P. Coroner's autopsy, acute purulent peritonitis

TABLE VII—CONT'D

PATIENT	CHARACTER OF DELIVERY	ONSET OF PUERPERAL FEVER	CLINICOPATHOLOGIC DIAGNOSIS	T.P.R. DAY P.P.	BLOOD COUNT	BACTERIOLOGY CERVIX	GENERAL THERAPY NO ANTITOXIC SERUM	RESULT AND COMMENT
R. G. W. 24 P. VI	Precipitate delivery	Second day P.P. headache, chills, and fever	Acute endometritis, metritis	Second day 103 - 96 -20	11,750	Strept. hem.	General measures on fifth day	Puerperal fever for two months after first child. Fever subsided P.P. Recovery
M. L. W. 31 P. III	Spontaneous (home by M.D.)	Ninth day P.P. chills, fever Vomited for 2 days Suprapubic pain	Acute metritis, pelvic peritonitis, septicemia	Fifth day 100^{6}- 122 -30		Strept. non-hem. in blood	Stimulants	Died on eighteenth day P.P. Chronic nephritis also present
M. La. W. 40 P. VIII	Spontaneous abortion at home, 4 months pregnant	First day fever, vaginal bleeding	Acute endometritis, secondary anemia	Fifth day 101^{8}- 120 -24		Strept. hem. Staph. albus. B. coli.	Stimulants. Blood transfusion, curettage	Recovery, home twelfth day P.P. Returned thirty-eight days later because of vaginal bleeding, curettage, home five days later
M. B. W. 23 P. I	Self-induced abortion, (slippery elm)	Second day P.P. Pain in lower abdomen, chills, fever, vomiting and vaginal bleeding	Acute metritis, pelvic peritonitis, septicemia	Fourth day 103^{2}- 152 -36		Strept. hem. in blood	General measures	Died ninth day P.P. Coroner's autopsy, acute purulent peritonitis

TABLE VII—CONT'D

PATIENT	CHARACTER OF DELIVERY	ONSET OF PUERPERAL FEVER	CLINICOPATHOLOGIC DIAGNOSIS	T.P.R. DAY P.P.	BLOOD COUNT	BACTERIOLOGY CERVIX	GENERAL THERAPY NO ANTITOXIC SERUM	RESULT AND COMMENT
A. B. C. 40 P. VI	Spontaneous abortion (home)	First day chills, fever, cough	Acute metritis, parametritis, pelvic peritonitis No pulmonary path. Arthritis of right ankle Sixth day P.P. Septicemia	Fourth day 102 - 112 -26		Strept. hem. in blood	Fifty-fifth day P.P. incision and drainage of right ankle	Recovery, ankylosis of right ankle. Home one hundred and thirty-fifth day P.P.
A. B. W. 28 P. I	Spontaneous (home by M.D.)	Seventh day P.P. Pain in left lower abdomen, chills, fever and cough	Acute endometritis, pelvic peritonitis, becoming diffuse Bronchopneumonia Septicemia	Twenty-sixth day 101^{2}- 148 -40	28,600	Strept. hem. also in blood	Twenty-fifth day P.P. 20 c.c., 1% mercurochrome intravenously. Leucocyte extract intramuscularly	Died thirty-fifth day P.P. No autopsy
B. C. W. 30 P. III	Spontaneous (home by midwife)	Sixth day P.P. Chills, fever	Acute metritis, parametritis, septicemia, arthritis of left hip joint	Ninth day 102 - 144 -32	5,500	Strept. hem. also in blood	General measures	Died thirteenth day P.P No autopsy
C. L. C. 20 P. II	Spontaneous 11° 20′	Third day abdominal pain, fever	Acute metritis, parametritis, pelvic peritonitis	Fourth day 102^{4}- 132 -28	23,100	Gram-positive strept. on smear	General measures. Twenty c.c. commercial antistrept. serum intramuscularly on eighth day P.P.	Condition not improved after serum. Fever subsided on twenty-first day P.P., recovery
C. K. W. 38 P. VI	Induced abortion (home, vaginal pack)	First day P.P. Fever, pain in lower abdomen	Acute metritis, parametritis, pelvic peritonitis, septicemia	First day 101 - 124 -22	11,400	Strept. hem. in blood	Sixth day P.P. 12 c.c. milk intramuscularly. Ninth day P.P. 30 c.c., 1% mercurochrome intravenously. Eleventh day P.P. 30 c.c., 1% mercurochrome intravenously	Septic course unchanged by mercurochrome. Developed bronchopneumonia. Died twentieth day P.P.

curred in 30 per cent of the cases while with the concentrated serum only about 5 per cent of the cases show serum sickness in three to seven or even twelve days after the injection. In the beginning of this study, the dose necessary to overcome the toxemia was unknown and amounts varying from 20 c.c. to 160 c.c. (in divided doses over several days)

TABLE VIII. COMPARISON OF MORTALITIES IN PUERPERAL FEVER

	NUMBER OF PATIENTS		SERUM-THERAPY	CONTROL (NO SERUM)
Fitzgibbon and Bigger	57			51%
Bailey	13		15.3%	
Warnekros et al	200		0.0%	
Gaessler	400		5.0%	
British	104	Other measures	72.0%	
Congress report	47		76.5%	
Krongold-Vinover	46		13.0%	
Lash	20	Endometritis	5.0%	
	20	Parametritis	25.0%	
	10	Peritonitis	90.0%	
	57	All stages	32.0%	
	13			61%

were given. However, it has been determined from clinical experience that 40 c.c. of the concentrated serum is an adequate initial dose, which can be repeated in this or half of this amount on successive days if fever and toxemia persist. In the presence of a marked toxemia, large doses of antitoxin are indicated, and should be introduced cautiously by the most direct route, that is, intravenously. The antitoxic serum in most instances regardless of the extent of the pathology overcame the toxemia, leaving the patient feeling well. In the presence of uncomplicated endometritis the fever as a rule also subsided but where a more advanced stage of the infection occurred, the temperature tended to remain unaltered. This observation would seem to confirm the theory that streptococcus antitoxic sera neutralize the toxins and aggressins of the bacteria, thereby allowing the leucocytes to render the organisms innocuous.

An analysis of the cases described in the tables shows that in the series of 20 endometritis cases, there was a mortality of 5 per cent. As the patient died two and one-half hours after the injection of the antitoxin the question arose as to whether the result could be ascribed to a reaction due to the serum or to an overwhelming infection. The large number of streptococci and the defense reaction of the tissue can be seen in Fig. 4, and the temperature curve in Fig. 1 *b*. Of the 20 women having parametritis with acute endometritis, 5 died, giving a mortality of 25 per cent. Patient C. K., who received the antitoxic goat serum on the twenty-sixth day postpartum, when irreparable damage had already been done, can hardly be considered a true test case. Anemia

resulting from delivery and later venesection for hypertension contributed to the death of patient B. P. In patient D. M. the bacillus colon was the predominant organism which was also isolated from the pus of the pelvic abscess. Although serotherapy was started early (fourth day postpartum) in the course of the infection of patient D. W., it was ineffective presumably because the predominating bac-

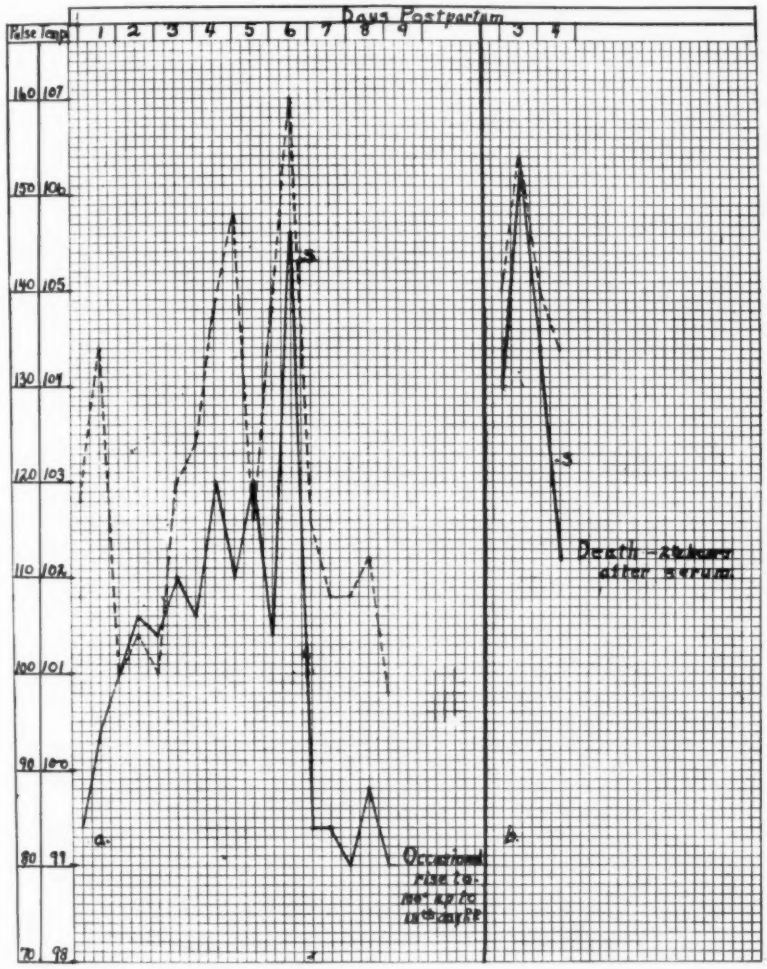

Fig. 1.—Puerperal fever: Acute endometritis septicemia. (Solid line, temperature; broken line, pulse.)

a. G. W. (See Table I.) *S*, 20 c.c. Puerperal fever streptococcus antitoxin intravenously.

b. E. W. (See Table I.) *S*, 40 c.c. Puerperal fever streptococcus antitoxin intravenously.

teria were Bacillus colon and Staphylococcus albus. The probable incompatibility of the blood used in the transfusion of patient R. G. played a rôle in causing her death. Fig. 2 illustrates the temperature and pulse curves of two patients with parametritis after serotherapy.

In the generalized or diffuse peritonitis, 9 of the 10 patients died, giving a mortality of 90 per cent. The surviving patient had a beginning diffuse peritonitis although she was very sick when admitted to the hospital. One of the 3 patients with thrombophlebitis and 2 of the 4 with pulmonary pathology secondary to that of the pelvis died. The degree of morbidity following antitoxin administration depended on the presence or absence of other bacteria besides the streptococcus and upon the extent of the pathology. It is quite evident that the serum does not influence directly the damage already done. From the percentages quoted, although not obtained from a large series of cases,

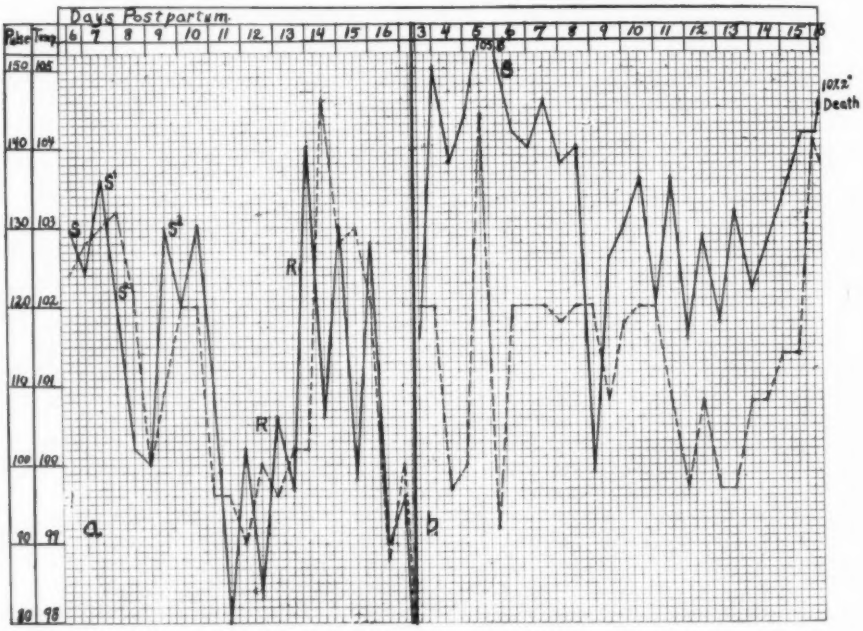

Fig. 2.—Puerperal fever: Acute parametritis septicemia. (Solid line, temperature; broken line, pulse.)

a. L. M. (See Table II.) *S*, 40 c.c. Puerperal fever streptococcus antitoxin intravenously. S^1, 40 c.c. Puerperal fever streptococcus antitoxin intravenously. 20 c.c. Puerperal fever streptococcus antitoxin intramuscularly. S^2, 40 c.c. Puerperal fever streptococcus antitoxin intramuscularly. S^3, 20 c.c. Puerperal fever streptococcus antitoxin intramuscularly. *R*, Onset of serum sickness, i.e. generalized urticaria and fever.

b. D. W. (See Table II.) *S*, 40 c.c. Puerperal fever, streptococcus antitoxin intravenously.

there is a definite impression that the antitoxin shows a definite value in the early cases of puerperal fever, that is, acute endometritis, less, when parametritis occurs, little or no value in diffuse peritonitis. The mortality of the whole group of patients (57) was 32 per cent.

In considering the control group of patients for comparison, the mortality was 61 per cent. Although all the patients had an endometritis before developing the more advanced stages, only 7 were ob-

served in the hospital. Of these, 3 died, giving a 43 per cent mortality. Four patients with generalized peritonitis died (100 per cent mortality). One of the 2, having a parametritis and septicopyemia died (50 per cent mortality).

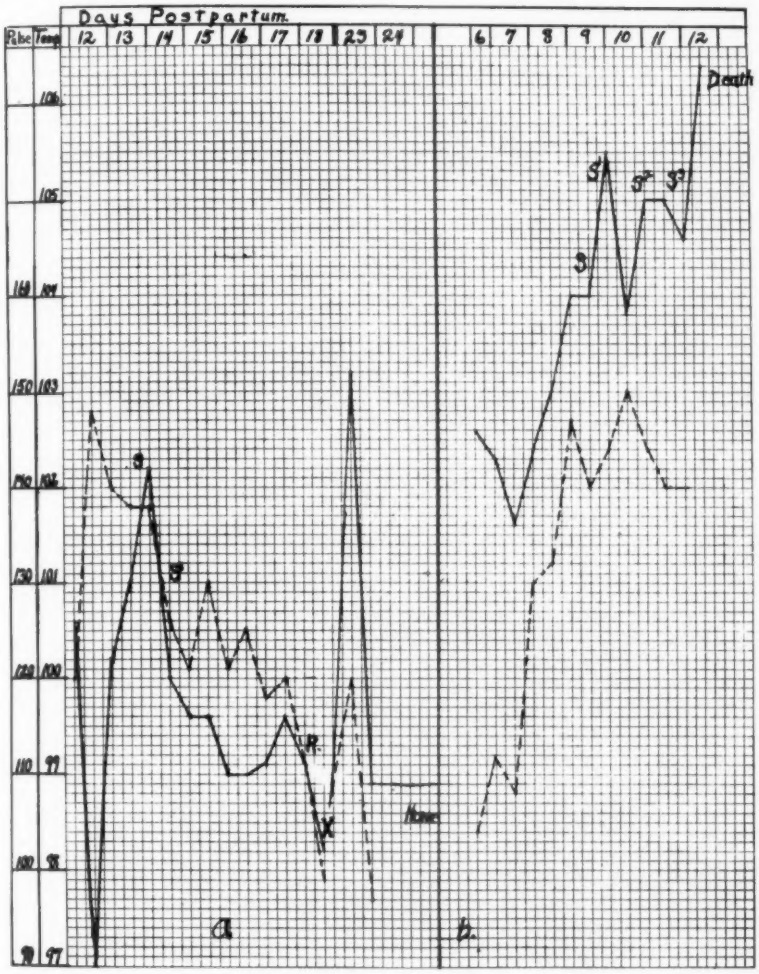

Fig. 3.—Puerperal fever: Acute generalized peritonitis septicemia. (Solid line, temperature; broken line, pulse.)

a. V. L. (See Table III.) *S*, 40 c.c. Puerperal fever streptococcus antitoxin intramuscularly. S^1, 20 c.c. Puerperal fever streptococcus antitoxin intramuscularly. *R*, Serum sickness. *X*, Interval of six days, temperature of 99°, followed by single rise to 103.2° with remission to 99°.

b, G. G. (See Table III.) *S*, 40 c.c. Puerperal fever streptococcus antitoxin intravenously. S^1, 40 c.c. Puerperal fever streptococcus antitoxin intramuscularly. S^2, 40 c.c. Puerperal fever streptococcus antitoxin intramuscularly. S^3, 40 c.c. Puerperal fever streptococcus antitoxin intramuscularly. 20 c.c. Puerperal fever streptococcus antitoxin intramuscularly.

Fitzgibbon and Bigger reported 57 cases of acute puerperal fever which occurred over a period of four years at the Rotunda Hospital, Dublin, with a mortality of 51 per cent. In this series, the hemolytic

streptococcus was present in 32 instances with a mortality of 47 per cent; the nonhemolytic streptococcus in 8 with a mortality of 50 per cent. One patient with an anaerobic streptococcus died (100 per cent

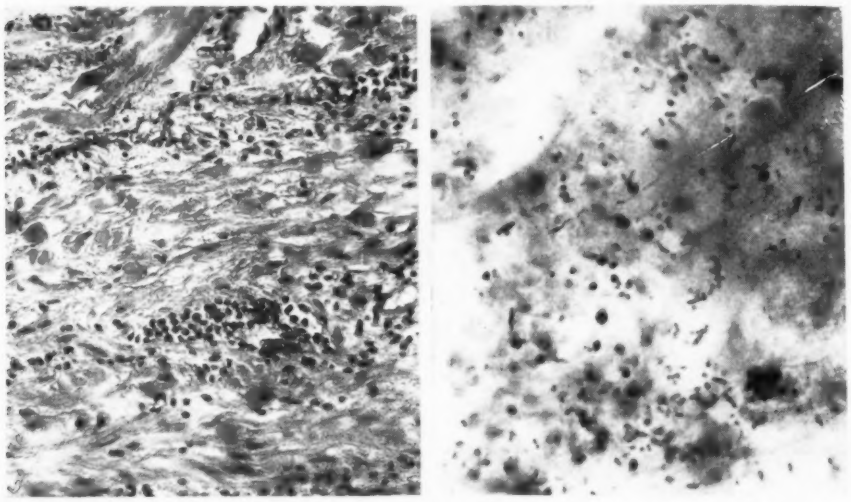

Fig. 4.—Photomicrograph from patient, E. W., illustrating the acute metritis (defense reaction) and the generalized invasion of streptococci.

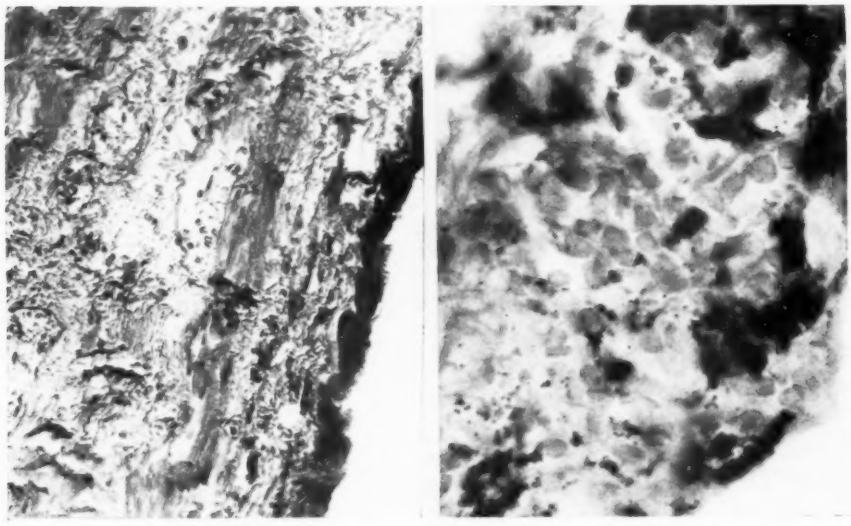

Fig. 5.—Photomicrograph from patient, G.G. (peritonitis), illustrating the poor defense mechanism in the uterus and the marked invasion of the subperitoneal space by the streptococci.

mortality). One of 6 patients with unclassified streptococci died (17 per cent mortality), and 2 of 3, in whom gram-positive cocci were seen on smear only, died (67 per cent mortality).

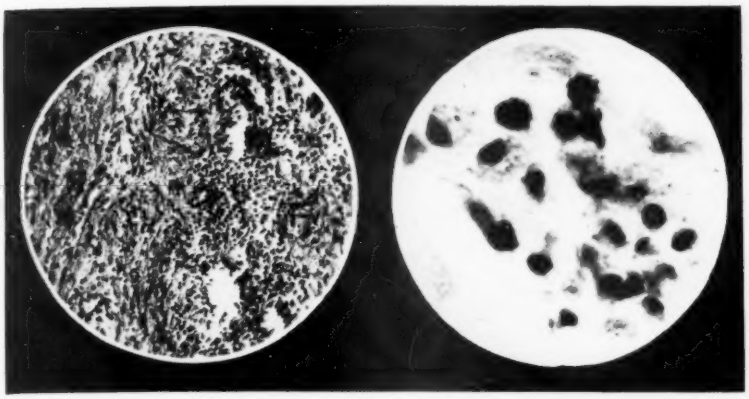

Fig. 6.—Photomicrograph from patient, B. G. (peritonitis-septicopyemia), illustrating the purulent phlebitis of the myometrium and phagocytosis of the streptococci.

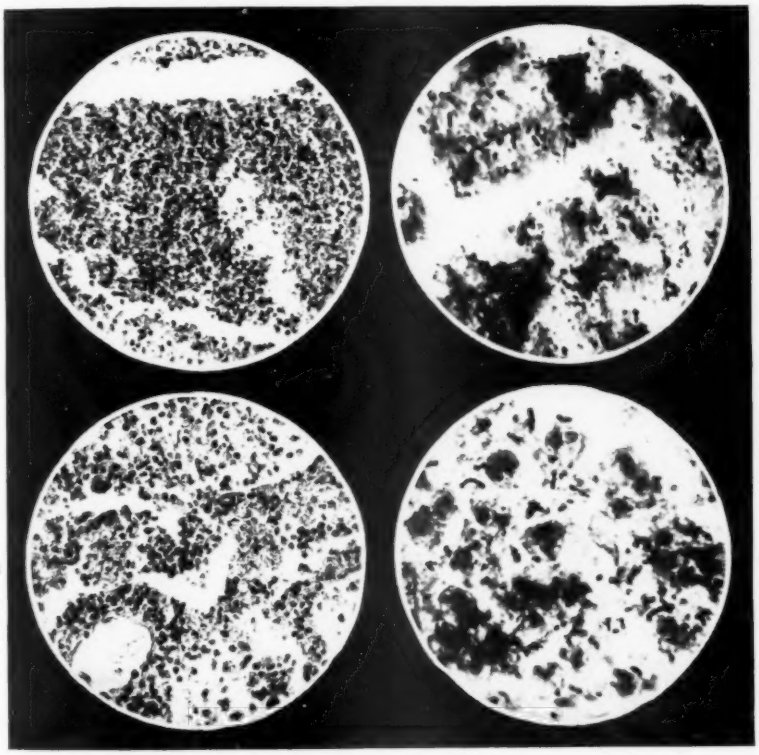

Fig. 7.—Photomicrograph from patient, J. M. (gangrenous purulent metritis), illustrating one of the many abscesses of the myometrium and the generalized streptococcal invasion and the associated bacteria. B. colon and Staphylococcus albus found in culture. *a*, From one of the abscesses of the lung, showing the presence of streptococci.

CONCLUSIONS AND COMMENT

The therapeutic value of an antitoxic serum is dependent on its specificity, potency and lack of serum reactions. The puerperal fever streptococcus antitoxin possesses specific value in acute endometritis with septicemia due to the hemolytic streptococcus. There is also a favorable response in the nonhemolytic streptococcus infections. Its potency as determined by toxin neutralization (Dick method) and by comparison with that of scarlet fever antitoxin of known therapeutic value shows a titer equal to that of the scarlet fever antitoxin. The antitoxic power increases with further immunization of the animals.

1. Small doses of the concentrated antitoxin achieving favorable clinical therapeutic results without immediate reactions is evidence of a specific rather than a nonspecific action.

2. Further evidence of the therapeutic specificity is adduced by the fact that with the increasing potency of the serum, correspondingly smaller doses were used with equivalent results.

3. The larger amounts of serum used in the earlier work were probably superfluous as the only index then used for the repetition of the dose was fever, rather than the condition of the patient.

4. To use fever as an only guide for serum-therapy may be misleading, since the antitoxin may overcome the toxemia and thereby allow the leucocytes to overcome the streptococci, without causing an immediate drop in fever.

5. In spite of the hyperpyrexia the general improvement of the patient influences the defense mechanism favorably permitting thereby the localization of the infection to the pelvis.

6. Immediate reactions are uncommon with the concentrated antitoxin and serum sickness occurs only when large doses have been used which are necessary at times. The serum sickness can be controlled by drugs.

7. In addition, the antitoxin is not harmful, having no irritating effect as no symptoms arose, indicating any disturbance of the kidney or other parenchymatous organ.

8. Since this antitoxin is comparable in its efficacy in the treatment of puerperal fever to diphtheria, scarlet fever or tetanus antitoxin, a woman developing symptoms of puerperal fever should receive it within thirty-six to forty-eight hours after the onset. Just as antitoxin is of little, if of any, value in far advanced diphtheria, tetanus, in sinusitis or peritonitis, in scarlet fever, so with advanced puerperal fever the administration of antitoxic serum is practically valueless.

9. Since severe and even fatal cases may appear mild at the onset and since heretofore there has been a tendency to withhold the anti-

toxin until it is apparent that the prognosis is unfavorable, it is well to give the antitoxin in all early cases.

10. The comparison of mortalities in the group of patients receiving antitoxin (32 per cent) and the control groups (Lash, 61 per cent, Fitzgibbon and Bigger, 51 per cent), shows evidence of therapeutic value of the puerperal fever streptococcus antitoxin.

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(For discussion, see page 424.)

Mayer, A.: Untimely Rupture of the Membranes, Monatsschrift für Geburtshilfe und Gynäkologie, 1927, lxxvii, 307.

Since the war there has been an increased incidence of premature rupture of the membranes, especially in elderly primiparas. Mayer has observed that not only is this true but also the fact that frequently many days elapse between the rupture of the bag of waters and the onset of labor pains. He believes the cause of the premature rupture to be an abnormal friability of the membranes the etiology of which is unknown. Microscopic examination revealed no abnormalities. It is just as difficult to explain the long interval before the pains begin. Patients should be informed of this occurrence and advised to enter a hospital to avoid complications. Nothing is done or at most an attempt is made to start labor medicinally or thermically. No complications were noted in the author's cases either during labor or the puerperium and infection which was previously feared if one waited too long after rupture of the membranes seldom occurred. In the cases where infection did occur no attempt was made to terminate labor and excellent results were obtained by waiting. In cases of delayed rupture of the membranes the author noted that the fetal heart tones became less distinct and slower in rate and he believes that the persistence of the bag of waters produces cerebral compression with stimulation of the vagus.

J. P. Greenhill.

EXPERIMENTAL ENDOMETRIOSIS*†

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INTRODUCTION

THE uncertainty surrounding the origin of endometriomas has given rise to a great deal of discussion. There is perhaps no subject in the whole field of gynecology concerning which more divergence of opinion has been expressed than that of heterotopic or misplaced endometrial tissue.

Our knowledge of endometrial proliferation dates back to 1860 when von Rokitansky[1] first described adenomyomas as pathologic entities. This important contribution was lost sight of for more than thirty years and it was only after von Recklinghausen[2, 3, 4] published the results of his studies in 1893, 1895, and 1896. that interest was revived. In 1895 von Recklinghausen published his famous Wolffian theory in an attempt to explain the etiology of adenomyoma. Among the earlier workers are Chiari,[5] Martin,[6] and Orthman. From the terms given this condition, namely, adenomyosalpingitis, adenomyositis tubae, and salpingitis isthmica nodosa, it is apparent that they were interpreted as basic inflammatory processes.

Chiari[5] in 1887 described a nodular swelling of the Fallopian tubes which he called salpingitis isthmica nodosa, a condition now known as adenomyoma of the tubes.

Cullen,[7-15] the outstanding American authority on adenomyoma, began the study of this subject contemporaneously with von Recklinghausen, and from the very outset up to the present time he has maintained unswervingly that all adenomyomata arise from müllerian rests or directly from the uterine mucosa.

In 1897 Pick[16] described the cell arrangement of these organoid tumors as identical with those present in the mesonephros or pronephros but later showed an inclination to the dual genesis, namely the Wolffian body and duct.

Robert Meyer[17] in 1897 ascribed the origin of the cornual tumors to the Wolffian body. In 1903 he[18, 19] still championed the von Recklinhausen theory and stated, "It is true that the normal tubal mucosa has no glands, but the pathologic tube is different, it can produce them." In 1909 Meyer[20] propounded an additional histogenesis, namely the intestinal mucosa (hypoblastic origin), but later withdrew in favor of the serosal theory and also declared the Wolffian body theory to be "a myth that is dying very slowly."

Iwanoff[22] in 1898 regarded the subserosal adenomyoma of the uterus as a transformation of peritoneum into the gland structure. He is supported in this view by Aschoff and L. Pick.

Robert Meyer[21] is now the most ardent defender of the serosal theory and goes so far as to say that celomic epithelium is of such quality that it can produce endometrial tissue in spite of the fact that endometriomas have never been found in the pleural or pericardial cavity. More recently he describes heteroplasia on the basis of congenital predisposition and dependent on ovarian activity or other stimulating influences. He considers this a sufficient explanation for endometriomas

*Read at a meeting of the New York Obstetrical Society, October 9, 1928.

†This work has been conducted under a grant from the Douglas Smith Foundation for Medical Research in the University of Chicago.

being found in the tube. Exception is taken with Halban's theory of lymphatic permeation on the basis that elastic tissue is not present in the uterine mucosa but is present in ectopic endometrioma-like tissue, and therefore the latter could not have originated from the endometrium. It should be borne in mind that contrary to this view, Lochrane has found elastic fibers present in normal uterine curettements. And what is more difficult of explanation is the correct interpretation of endometrial glands in lymph nodes reported by Emil Ries,[24] Wertheim and Wulfing.[25]

This theory is in direct conflict with Cullen's explanation of uterine adenomyomata which he has proved conclusively arises by direct extension of the uterine mucosa.

We also note that Russell in 1899 reported a case of adenomyoma of the ovary and considered this as an anomalous point of development of a portion of müllerian duct in the germinal epithelium.

In 1918 Lockyer[26] published his work on "Fibroids and Allied Tumors" with an extensive review of the literature of adenomyomata up to that year. He was a fervent adherent of the mesonephric teachings and considered Kossmann's[27] work on müllerian origin of these tumors as destructive criticism, in spite of the fact that the opinions of Kossmann and Cullen are supported by Baldy and Longscope,[28] Opitz,[29] Gottschalk,[30] Klages[31] and Lockstaedt.[32]

Ewing[33] in 1918 described adenomyomas present in the broad and round ligaments, groin, vaginal wall, Fallopian tube and rectum.

In 1921 Sampson[34] published his first paper on endometriomata and discussed the perforating hemorrhagic (chocolate) cysts of the ovary. It was due to the meritorious work of Sampson that this renewed interest in endometriomas was aroused in the gynecologic field with a notable academic revival and discussion of their etiology. This author postulated that endometriomas were derived from uterine mucosa which reached the ovary via the Fallopian tubes or through the lymphatics. The viability of desquamated endometrial epithelium has been seriously questioned on account of the necrosis and necrobiosis of the surface endometrium in menstruation resulting from the lytic action of menstrual secretions as shown by O. Frankl.[36] This also affects plant life as demonstrated by Schick;[37] and Macht and Lubin[38] have also isolated a menotoxin from the menstrual discharge.

Robinson[35] in a masterly critical review on the histogenesis of heterotopic endometrial proliferations questions very seriously Sampson's views on implantations of desquamated endometrial epithelium. Cron and Gey[39] find that the menstruating endometrium is not only viable but can be grown in tissue cultures.

The dissemination of endometrium through the tubes will require further proof in spite of the fact that endometrial particles have been found free in the lumen of the tubes. E. Novak[40] in his studies of ovarian metastasis from primary carcinoma of the uterine body has often observed free cancer masses in the lumen of the tubes but interprets this finding as a downward movement toward the uterus rather than upward toward the peritoneum. With more careful study of lymphatics the so-called "implantation" and "contact infection" by new growths is viewed with increasing skepticism by many pathologists.

Van Oettingen and Luden[41] reported very striking findings in a series of twenty ovarian cysts containing endometrial tissue which they divide into a superficial group and a deep group. In the latter group they were able to trace the origin of the organoid tumors to the ovarian epithelium and concluded that since it had a definite connection with the surface of the ovary, Sampson's theory was incorrect. In a study of ovarian endometriomas by Semb,[45] the follicular epithelium is considered the source (histogenesis) of these endometrial growths.

Heany[42], Danforth[43], Schochet[44], and Selig have reported implantation endometriomas in the abdominal wall and appendix.

Additional citations of the clinical literature of papers on endometriosis, except for the experimental contributions, are omitted, as this will only mean futile reiterations of the conflicting theories of etiology without adding any definite data or clearer understanding of the problem.

EXPERIMENTAL ENDOMETRIOSIS

In spite of the great amount of experimental research upon the subject of tumor formation, no one has yet devised a method by which tumors of any organ in any known animal can be induced at will. Efforts to produce endometriomas have passed several phases suggested by theoretical views. Transplantation of adult tissue was early found by Zahn[46] and Leopold[47] to result in eventual and usually prompt absorption. Lengemann[48] followed the fate of misplaced cells and concluded that misplacement alone, hyperemia, or partial degeneration of the cell mass was not sufficient to produce tumor growth. However, Nichols[49] in his extensive series of tests found uterine epithelium to undergo definite proliferation. Ribbert implanted portions of organs in the peritoneum, and although they functioned for a time in these new positions, yet they eventually atrophied.

Stillings[50] in 1909 transplanted successfully fragments of the uterus into the spleen of rabbits with subsequent cyst formation.

Schochet[51] in 1914 in a series of transplants of ovary in the anterior chamber of the eye failed to note a hyperplasia or metaplasia of the surface epithelium of the ovary or peritoneum into endometrial-like tissue. Hesselberg, Kerwin and Loeb[52] successfully transplanted endometrium into the ear of the guinea pig.

Evidence for growth stimulation by chemical agencies is furnished by the proliferation and hypertrophy which takes place in the uterus[53] and mammary gland during pregnancy. Robert Frank[54] produced similar changes with lipoid fractions of extract of placenta and corpus luteum. Frank[55] has shown that transplanted bits of uterine tissue are stimulated to grow by these substances thus excluding a nervous control of growth.

In 1922 Jacobsen[56] reported successful autotransplantation of endometrium in the peritoneal cavity of the rabbit. This work has been confirmed by Katz and Szenes[57], Blair Bell[58] and Dossena[59] on the rabbit, guinea pig, and rat. These observations support Sampson's idea that fragments of endometrium on reaching the peritoneal cavity may become implanted on various organs and grow. Similar successful implants in cesarean scars in the guinea pig and mesoappendix in the dog are reported by Schwartz[60], and O'Keefe and Crossen[61].

It is hoped that this short review and survey of the literature of experimental endometriosis will give the reader a proper perspective of the subject. While conflicting views of the etiology of endometriomas have been cited, this should not obscure our subject matter but make us realize that we are embarked on the fog-bound and uncharted sea of tumor formation and that we are likely to fix our attention on simple variables with information of little intrinsic value and that we are likely to lose our bearings.

MATERIAL AND TECHNIC

Virgin female guinea pigs supplied by the local dealers were used in this study. In most instances two or three estrous cycles were recorded for each animal before the experiments were performed. In this manner definite data were available to permit us to operate in the proestrous stage. In our earlier experiments rabbits were used, but after nine months of study we came to the conclusion that estrous cycles could not be followed in this form and that the rabbit was not a suitable animal for this particular phase of study.

In our later studies the guinea pig was the only animal used, as there is a definite rhythmical "heat period" in this animal. The estrous

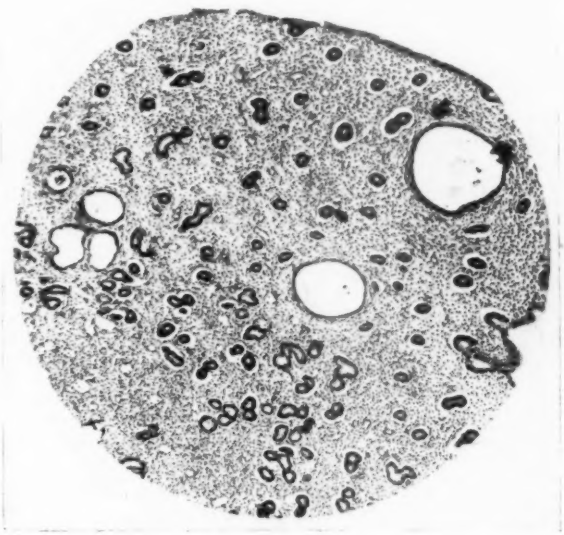

Fig. 1.—Diestrum, period of rest. Tenth day. 60x.

cycle in the guinea pig has been solved by the epochal work of Stockard and Papanicolaou.[62] Our observations are in accord with these authors but for few exceptions which are noted in the descriptions of the stages, which are taken almost verbatim from their publications. We repeat in part their descriptions of the normal stages of the cycles to present more clearly our findings of the transplants. The terminology is that proposed by Heape[63] and adopted by Marshall[64] and others. "Proestrous, the first part of the sexual cycle; estrous, especial period of desire in the female; metoestrum, the short period when the activity of the generative system subsides and the resting condition is resumed in case conception does not occur; diestrum, the short period of rest between cycles. These four periods, the proestrum, estrum, metoestrum and diestrum are known as a diestrous cycle. Guinea pigs

kept in a state of domestication and under uniform environmental conditions possess a regular diestrous cycle repeating itself in the nonpregnant female about every sixteen days. During each cycle typically corresponding changes are occurring in the vagina, the uterus, and the ovary. Each period of sexual activity lasts about twenty-four hours and is characterized by the presence of a definite vaginal fluid which is easily observed by examination on the interior of the vagina. From six to twelve hours or even more, the secretions are of a mucous consistency (proestrum). The second stage is characterized by a thick cheese-like substance (two to four hours) which finally becomes slowly liquified and serous (four to six hours). The fourth stage is the shortest, only one or two hours long, and is characterized by the presence of

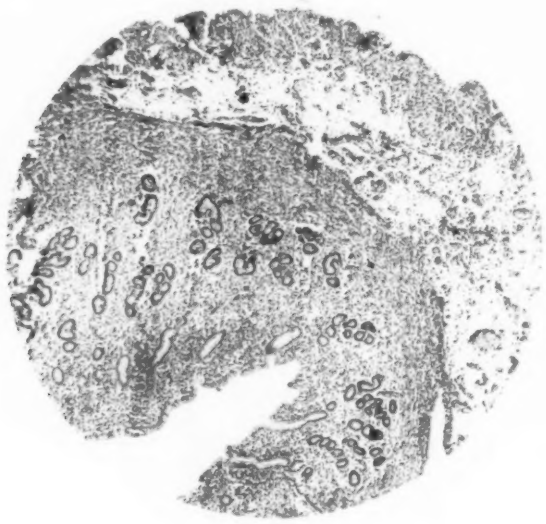

Fig. 2.—Proestrum, first part of sexual period. 70x.

blood." In our series of 80 guinea pigs we failed to note the presence of blood except in very few instances. In animals killed in the fourth stage in only one instance did we observe the presence of free blood below the epithelial layer. In many instances we noted the presence of an epithelial cast of the upper part of the vagina which could be removed with tissue forceps.

"During the sexual period of twenty-four hours the organs are congested, the blood vessels tortuous and dilated, and the mucosa is of a darker red hue which soon disappears after the estrous period."

In the course of our experiments it was noted that the vessels in the transplants showed a periodic rhythmic contraction. This phase of the problem was delegated to my associate, J. E. Markee, who has carefully studied the changes during the cycle.

HISTOLOGIC STRUCTURE OF THE UTERUS

The epithelial layer of the uterus in diestrum is of a ciliated cuboidal type. Mitotic figures are not present in this stage. Cyst formation is frequently observed about the tenth day of the cycle. The blood vessels are small; the stroma shows very few wandering cells, except for a few leucocytes (Fig. 1).

In the proestrous stage the epithelial layer is tall columnar in type, closely packed, giving the appearance of a pseudostratified layer. The cells contain much secretion, and small extrusions or knobs of secretion can be seen in the lumen of the glands. The capillaries in the stroma are congested, and migration of leucocytes is often seen (Fig. 2).

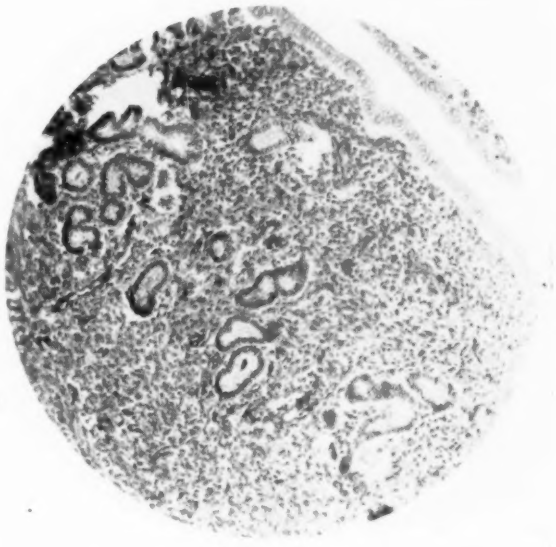

Fig. 3.—Estrum, period of desire. 140x.

In the estrous period the vessels are more congested; mitotic figures are frequent, and collections of polymorphonuclears beneath the epithelial cells are frequently observed (Fig. 3).

RHYTHMIC CAPILLARY CONTRACTIONS IN THE TRANSPLANTS

These observations of capillary changes are included in this paper as they were observed in our experimental endometrial transplants. It is difficult to interpret their true significance or their relationship to the menstrual cycle.

SUMMARY BY J. E. MARKEE

The vascularity of the uterus of the guinea pig undergoes cyclic variations that make it appear to blush and blanch. Both the speed and the extent of these vascular changes are affected by the time of

day and the stage of the estrous cycle. We have been unable to find similar vascular changes in any other tissue, either in situ or in transplants to the anterior chamber of the eye, of pancreas, islands of Langerhans, vas deferens, uterine muscle, heart muscle or liver. It is possible to make much detailed observations on endometrium transplants into the anterior chamber of the eye. The blanching and blushing can be studied by means of a binocular microscope. By comparison with a Tallqvist hemoglobinometer we found that the two colors were comparable with the colors indicated by 0 and 60 per cent hemoglobin respectively.

We made twenty-minute records every two hours for three complete estrous cycles of sixteen days each. Two of the records were made on one animal and one on another. Kymograph records were made of the color changes by means of a graduated dial and a muscle lever.

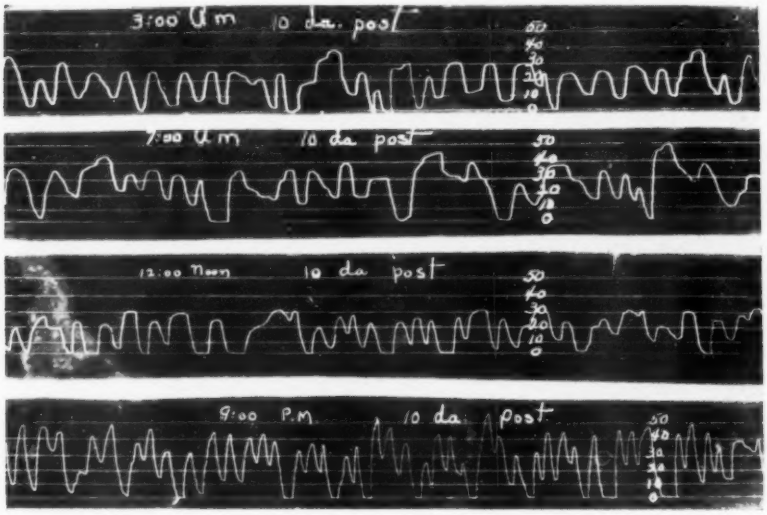

Fig. 4.

The first group of kymograph records illustrates the four typical phases of the vascular reaction seen every day of the estrous cycle except during estrus. The first record was taken in the early morning. The vascular changes occurred about every twenty seconds; the average color was about 25 per cent hemoglobin, and the transplant was completely blanched or white about 6 per cent of the total time. In the forenoon both the speed and the extent of the reactions are increased. At this time they recur about every fifteen seconds; the average color of the transplant is considerably above 30 per cent hemoglobin and it is completely blanched about 10 per cent of the total time. From noon until 3 P.M. the speed and especially the extent of the vascular changes are greatly decreased. They recur about every eighteen or nineteen seconds. The time in complete blanch is less than 10 per cent of the total time and the average color is about 25 per cent hemoglobin. The height of the vascular activity is reached in the late evening from about 8:00 P.M. until 11:30 P.M. The vascular cycles recur about every twelve or thirteen seconds. The amount of time in complete blanch is

more than 12 per cent and the average color is about 35 per cent hemoglobin. These four phases: the lowest activity in the early morning, an increase in the forenoon, a slight decrease about noon and the height of the activity in the evening, are found throughout the cycle except during estrus. (Fig. 4.)

The second group of kymograph records illustrates the effect of estrus on these vascular changes. The first record illustrates the condition during proestrus. Two hours before this record was taken, the vascular changes were recurring every thirteen seconds, and the transplant was completely blanched 16 per cent of the total time. When this record was taken, the changes were recurring every twenty seconds and the amount of time in complete blanch had dropped to about 8 per cent. There was a decrease of about 40 per cent in the vascular activity of the transplant during this two-hour period. At this time of day there would normally have been an increase. The second record illustrates the condition during the whole of estrus. This animal was

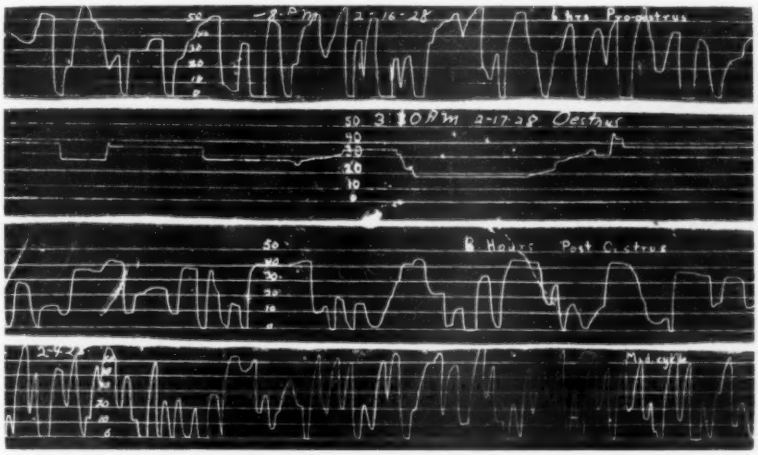

Fig. 5.

in estrus as determined by the vaginal smears and other methods from 2 A.M. until 7 A.M. There were no vascular changes that compared in extent with those found at all other times in the estrous cycle. The color of the transplant for this five-hour period remained around 25 per cent, neither falling much below 20 per cent nor rising much above 35 per cent.

The third record illustrates the condition during postestrus. The vascular cycles reappear at this time, and there is a very rapid return to the condition found during the diestrum. However, the long plateaus at about 40 per cent hemoglobin are typical of this stage. The last record illustrates the height of activity reached during the diestrum when the vascular reactions sometimes recur every twelve seconds, the average color of the transplant is above 35 per cent hemoglobin, and the transplant is completely blanched 16 per cent of the total time. (Fig. 5.)

After training an animal to sit still we were able to observe the capillaries through a microscope. The small blood vessels in the transplant

alone appeared and disappeared about every fifteen seconds while the blood vessels leading to the transplant as well as all the other vessels in the eye remained unchanged.

We have been unable to observe this phenomenon in well-vascularized transplants of uterus in immature animals.

The facts briefly summarized are: These vascular changes are influenced by the time of day, being at their lowest ebb in the early morning, increasing both in speed and extent in the forenoon, decreasing again about noon and reaching their height late in the evening. They are also influenced by the stage of the estrous cycle, slowly during proestrus until they disappear completely at the time of estrus and then reappear rapidly in postestrus. These gross changes are caused by great variations in the amount of blood in the capillaries and arterioles.

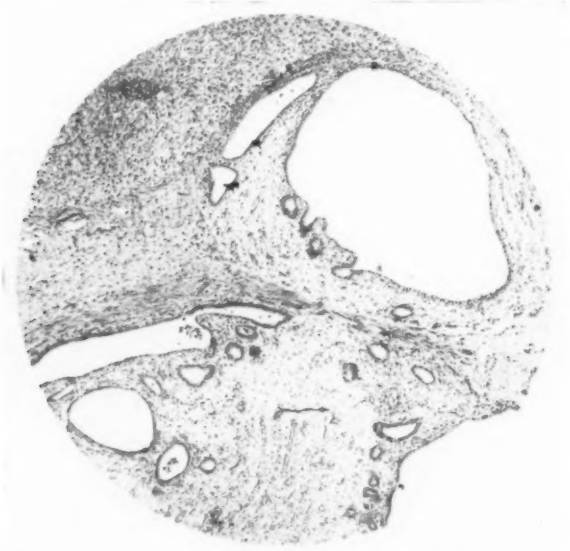

Fig. 6.—Uterine transplant in liver of rabbit No. 4, nine months after transplantation. Note cyst formation. 60x.

EXPERIMENTAL TRANSPLANTS

Series I, Normal Controls. Group A.—In this series five female guinea pigs were used. The animals are in proestrous stage. Under ether anesthesia and strict surgical asepsis the abdomen is opened by a low midline incision measuring three-fourths of an inch. The left horn of the uterus is excised, bleeders in the broad ligament are ligated, raw surfaces covered with peritoneum, and the abdominal cavity is closed in layers with linen sutures. A second midline incision is made in the upper part of the abdomen below the ensiform cartilage. The left lobe of the liver is delivered through the incision and a small longitudinal section of the uterus is implanted into the liver substance. In two of the controls transplants were also made into the spleen and subcutaneous tissues. To identify these transplants, we placed a small knot of black thread in one of the corners of the transplant. The remaining part of the uterus was fixed in formol-zenker solution for microscopic study.

Group B.—In this series transplants were made in the anterior chamber of the eye.

The animals were killed at varying periods of time and sections of the transplants and the remaining horn of the uterus sectioned and examined. In most instances the animals were killed after three months with the exception of one

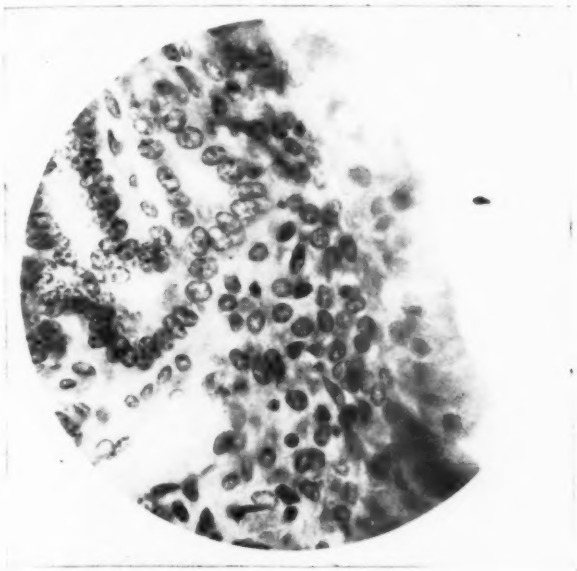

Fig. 7.—Metaplasia of uterine epithelium, or a degenerative process in eye transplant.

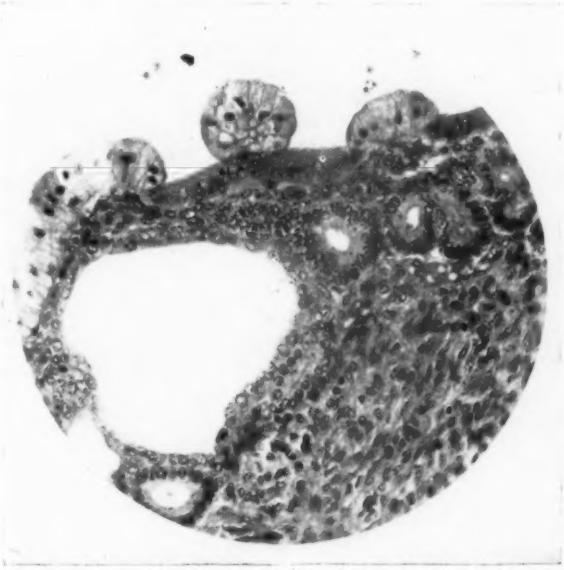

Fig. 8.—Metaplasia of uterine epithelium of eye transplant. Transplanted seven months before animal was killed. 290x.

guinea pig and two rabbits from our first group of experiments. Rabbit No. 4 was killed nine months after making transplants in the liver and spleen.

We found like many other investigators that the untreated endometrial transplants were eventually absorbed without active proliferative growth except for cyst formation in the rabbit No. 4 as seen in Fig. 6 and in group *B* of eye transplants. In those animals in which early vascularization of the transplants takes place, the endometrium is not absorbed after several months. In one of the animals of this group there was a metaplasia of the uterine epithelium. The cells were larger, filled with secretion, the nuclei more vesicular, and in a number of the serial sections there was an apparent proliferation with a pseudopapillary arrangement or budding of the surface epithelium of the glands in the aqueous fluid of the eye (Figs. 7 and 8).

Series II. Scharlach R. Sudan III Ether Solutions.—It has been shown that cells treated or influenced by lipoid solvents tend to exhibit increased and atypical proliferation. In 1906 B. Fischer[65] introduced an interesting field of study by

Fig. 9.—Downward growth and proliferation of epithelium of vaginal mucosa after olive oil and scharlach R injection. 70x.

injecting under pressure a saturated solution of scharlach R in olive oil under the skin of rabbits' ears. After a few days there is a marked proliferation and downward growth of epithelium which resembles an epidermoid carcinoma, but the growth ceases when the oil has been absorbed. Since no such effect followed injection of olive oil, Fischer assumed that the dye contained a stimulating substance for epithelial growth. These observations have been verified by many investigators.

In *Group A* of this series we repeated these classical experiments with the vagina. There was a marked proliferation and downward growth of the epithelium of the mucosa, as seen in Fig. 9. Sections from these areas were then transplanted into the liver and anterior chamber of the eye. The epithelial cell of the mucosa continued to grow but formed only epithelial cysts and no atypical proliferation under these conditions. The cavity of the cyst is filled with cornified epithelium and débris. The wall of the cyst is lined by a stratified cuboidal epithelium as found in epithelial cysts in other organs (Fig. 10).

Group B.—Similar experiments were made with the uterus in situ in which the scharlach R was injected beneath the mucosa through the serous and muscular layers. After several days sections were transplanted into the liver and anterior chamber of the eye.

No additional evidence was noted in our experiments than found in the classical experiments of B. Fischer. The glandular epithelium remains intact but shows no evidence of further proliferation but rather absorption and fibrosis of the transplant.

In *Group C.* of this series we substituted a 1 per cent ether in physiologic salt solution. Pieces of endometrium were exposed to this lipoid solvent for varying periods of time prior to transplantation to the liver. Reinke[66] noted atypical epithelial growth after injecting a 4 per cent ether solution in the eye of a salamander. He then transplanted this proliferating epithelium to other salamanders. There was marked atypical proliferation in these grafts.

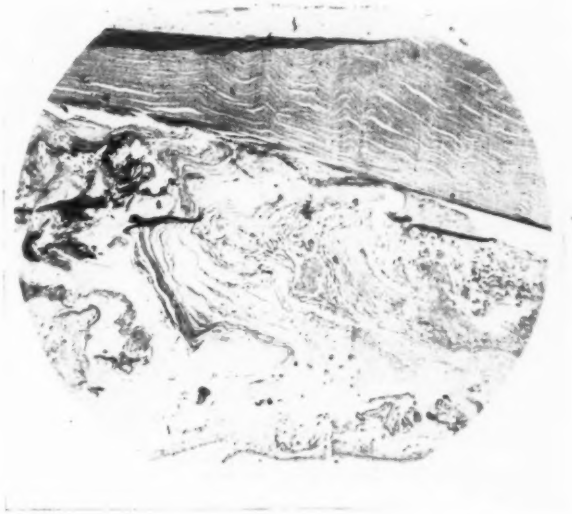

Fig. 10.—Eye transplant of vaginal mucosa after olive oil and scharlach R injection. Epithelial cyst with cavity filled with desquamated epithelium. 70x.

In our series of animals we obtained only negative results. Although the transplanted gland cells in the liver appeared more deeply stained, cystic, and showed mitotic figures, we were inclined to interpret this as a result of degeneration rather than active growth.

Group D.—In this series of experiments a modification of the scharlach r method is introduced. It has been shown that when lycopodium spores[67] are introduced into the body there is an extraordinary new formation of cellular fibrous tissue. With this idea in mind, lycopodium spores were added to the saturated scharlach R olive oil solution with the object of adding an irritant factor to the growth stimulus. With this method we obtained hyperplasia of the glandular elements and also an extensive new formation of cellular fibrosis; we were not able to interpret these factors as stimuli to growth. It is difficult to determine that this apparent proliferation is not reparative in compensation to degenerative and inflammatory changes, and therefore possibly obeying some other biologic law (repair to injury) than that of a simple reaction to a chemical irritating

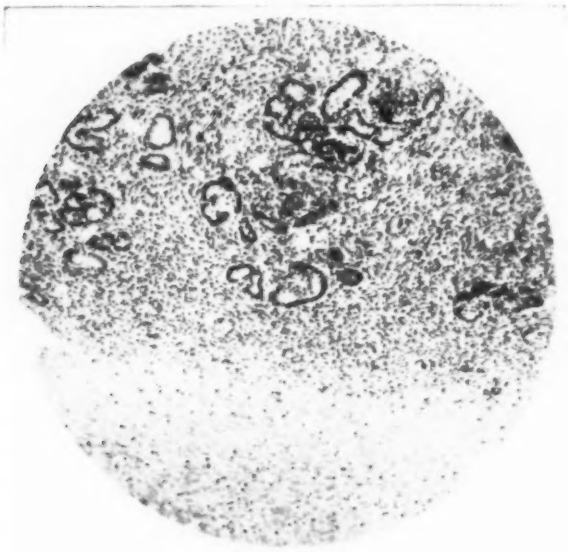

Fig. 11.—Endometrial transplant in liver after scharlach R and lycopodium. Note hyperplasia of glandular structure, giant cell formation (tubercles) and areas of degeneration. x140.

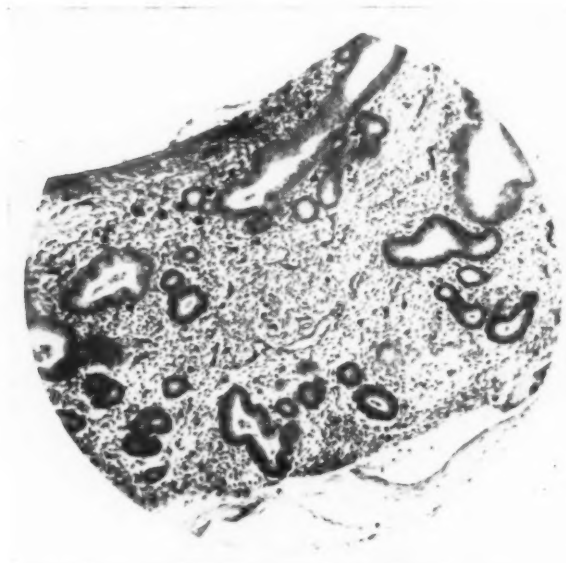

Fig. 12.—Effects of sensitization of mucosa of endometrium. Compare with Fig. 3, the control. There is a marked glandular hyperplasia which appears as an adenomatous growth with absence of any inflammatory process. (Cells of inflammation.) 110x.

stimulus. In Fig. 11 cellular proliferation and areas of degeneration (necrosis) are present while in other areas there is definite giant-cell formation with pseudotubercle formation. And in spite of this active reparative process, there was no marked cellular proliferation of the endometrial glands, which we are willing to

interpret as active hyperplasia and proliferation as seen in benign tumor formation.

Series III. Group A.—This group of experiments is based on the principle of Loeb's[68] artificial parthenogenesis and fertilization. He employs a hemolytic substance, acids, bases, et cetera, followed by a hypertonic solution. Our experiments are based on the principle of cell stimulation induced by variations of osmotic pressures of solutions and an oxidase to alter or change the physical condition of the cell wall. We shall not attempt at this time to make a detailed analysis of the principles involved but merely to give a short detailed description of one of the experiments. We are inclined to believe that this field of research will open new avenues of approach to cell growth.

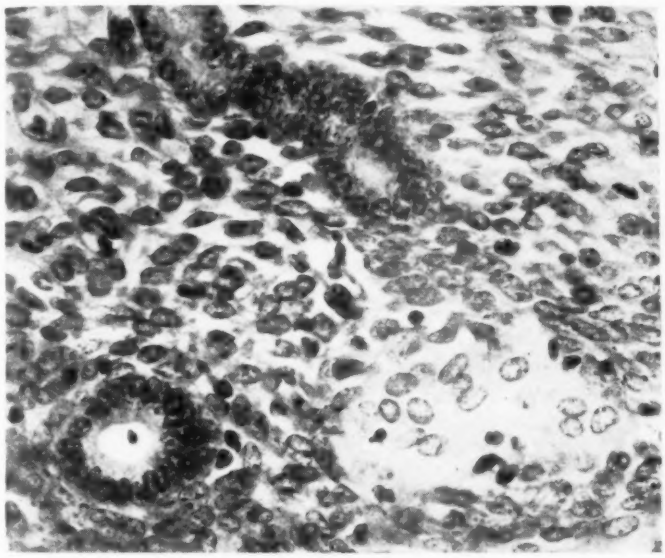

Fig. 13.—Syncytial formation from base of one of the glands from transplant. This condition has been observed in human endometrium following rapid growth of proliferating endometrium.

EXPERIMENT C 64

A mottled gray female guinea pig. Laparotomized June 11, 1928. The left horn of the uterus was excised and control fixed in formol-zenker solution. A small section of the mucosa was placed in an isosmotic solution of strontium chloride from 11:10 P.M. to 11:15 P.M.; transferred to rabbit's serum 11:15 P.M. to 12:08 A.M. and then placed in a hypertonic salt solution (12.5 grams sodium chloride solution to 1000 c.c. of water) from 12:08 A.M. to 2:02 A.M. Washed in Ringer's solution for one minute and then transplanted into the anterior chamber of the eye of this animal. The guinea pig was killed on 6/28/28. Fig. 3 is the control utilized in this paper to show the estrous cycle. Fig. 12 shows effect of sensitization.

Series III, Group B.
Series III, Group C.
Series III, Group D.
Series IV.

These groups are merely cited because Figs. 13, 14, and 15 were taken from some of the sections of these groups. A detailed description will be

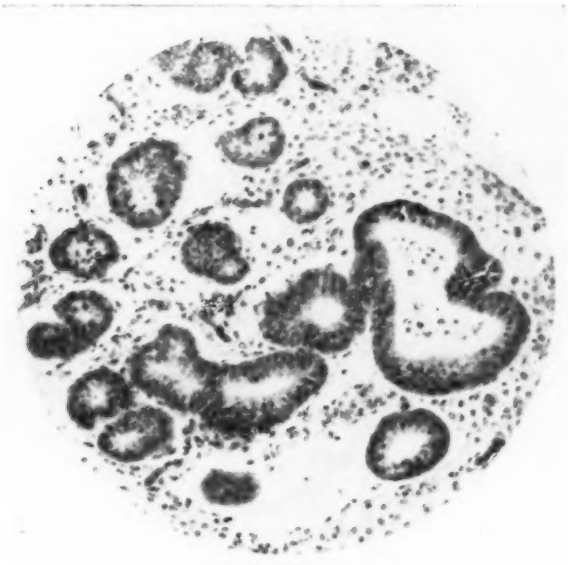

Fig. 14.—Marked glandular hyperplasia of endometrial transplant from the anterior chamber of the eye.

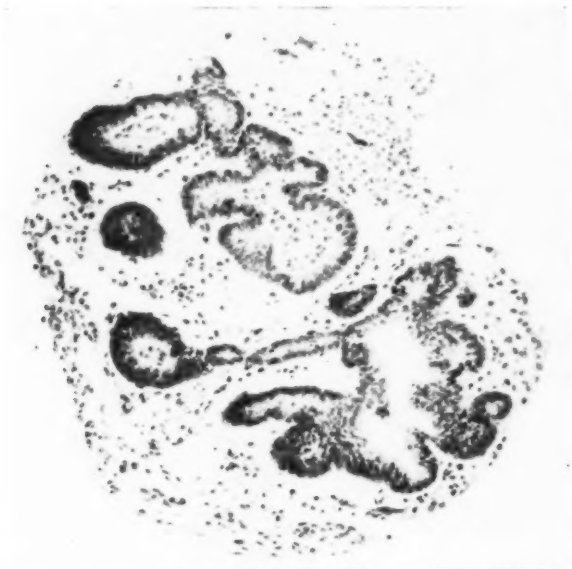

Fig. 15.—Similar to Fig. 14 taken from another area of eye transplant.

published when these experiments are completed. Fig. 13 shows a syncytium formation from one of the uterine glands. Figs. 14 and 15 showed marked hyperplasia of glandular tissues of transplants.

We choose to postpone the final conclusions of our work until the other groups of this series are completed.

The writer wishes to acknowledge his indebtedness to Dr. George W. Bartelmez under whose supervision this problem has been undertaken. To Dr. R. R. Bensley for many helpful suggestions and criticisms, and to Dr. James Ewing (New York) for his interpretation of sections of transplants. Thanks are due to Mr. J. E. Markee for assistance in the preparation of histologic slides.

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55 EAST WASHINGTON STREET.

(For discussion, see page 413.)

A STUDY OF THE USE OF PARATHORMONE IN THE CONTROL OF MENSTRUAL BLEEDING

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WE HAVE been trying for the past two years[1] to control excessive menstrual bleeding with the parathyroid hormone. The primary rationale of this treatment is based on the increased coagulability of the blood encountered in hypercalcemia.[2] Added to this was the possibility that hypodermic medication with the active principle of the parathyroids might indicate to us some of the relationship between the ovarian and parathyroid secretions.

Beginning with the work of Collip,[2, 3] investigators[1-4] have noticed the production of hypercalcemic states with the increased coagulability of the blood in laboratory animals, particularly dogs. This hypercalcemic state in dogs is characterized by anorexia, hemorrhage into the gastrointestinal tract, and death. According to Collip,[3] this danger may be imminent when a serum calcium of 15 mg. per 100 c.c. of blood is reached. Hueper[4] has reported depositions of calcium in excess of normal in many important organs obtained from dogs in which this hypercalcemic state has been maintained for some time.

As far as we have been able to ascertain no case has been reported of a fatality in the human nor has any one established a level of

hypercalcemia in man. In view of the experimental evidence and lack of established rules for dosage, we have had to be extremely careful in our experimental work on women.

It is difficult to evaluate clinical symptoms in different individuals, especially in women who are menstruating. Nausea, vomiting, headache, and a feeling of depression are a common accompaniment of the menstrual period. Therefore, we have discontinued medication in several instances where if we had had the courage to continue, more definite results might have been obtained.

METHOD

These experiments were conducted on a series of fourteen young women who complained of severe menorrhagia. All of them had been previously subjected, with only temporary if any results, to the usual hemostatic procedures, such as oxytocics, injection of foreign proteins, and operation. The foreign protein injections were given with the possibility in mind that the disturbance might be on an infective basis in spite of negative palpatory or operative findings. Eight of these patients had menstruated profusely from the beginning of their menstrual history. Subsequent observations are recorded in this paper on the four patients included in our preliminary report. Due to a change in services some of these patients have not been observed for the past nine months. However, the results include observations on most of them for at least three menstrual periods after all treatment had been discontinued. The research department of the Eli Lilly Company kindly furnished us with the parathormone used in all of these experiments.

RESULTS

CASE 1.—This patient is one on whom results have been recorded in the previous paper. Menstruation began at the age of ten. The first period was normal but the second period lasted twenty-one days and all subsequent periods have been profuse. She was first seen in our clinic at the age of eleven. She had been in the hospital six times for treatment, which included ergot, pituitrin, curettage, horse serum, and milk. Since that time she has been in the hospital for observation, four times for treatment with parathormone. Following the milk injections she had no reaction and there was some decrease in the amount of blood lost at the menstrual period but the effect did not last. When we began the parathyroid treatment the patient was seventeen years of age. She had been forced to give up her school work on account of general fatigue and loss of time at menstrual period. The periods occurred about every three weeks and lasted eight to nine days. During this time she used from twenty-four to twenty-eight large homemade menstrual pads.

We gave this patient forty units of parathormone (Lilly) intramuscularly, either alone or combined with large doses (180 grains) of calcium carbonate by mouth[6] each day during the menstrual flow. This treatment was continued throughout five periods during the latter half of 1926 and January and February of 1927. During this period of treatment blood was withdrawn each day before the parathormone was injected.

During the first four periods the blood calcium did not vary more than the variation we[5] have found to be normal for healthy women. The lowest calcium reading that we obtained in this period was 9.92; the highest 12.81. The intermenstrual periods during this time had lengthened to thirty or thirty-three days and the number of pads had decreased to twelve or fourteen. The patient had returned to school.

During August of 1927 we again treated the patient at period time during an extremely hot spell of weather. On the third day of the period following an injection of forty units of parathormone which had been repeated both of the preceding days and accompanied by 180 grains of calcium carbonate by mouth, the blood calcium rose to 13.42 per 100 c.c. The patient became very pale, nauseated, and complained of severe headache. The pulse varied from 120 to 140 per minute for several hours. The menstrual flow stopped. The clotting time determined by the capillary tube method decreased from three minutes to one minute, thirty seconds. Twelve pads were used during this period.

The patient has not received treatment since that time. The menstrual flow has gradually increased to its previous duration and amount. Four months ago the patient was married. She has not become pregnant neither has sexual contact varied the severity of the bleeding.

CASE 2.—This patient was also reported in our previous paper. Age twenty-six years. She began to menstruate at sixteen and was regular, twenty-eight day type which lasted six days, using eighteen pads. About June, 1925, the periods became longer, lasting at times two to three weeks. She was curetted February 18, 1926, but without relief. Pelvic findings were normal. Calcium variation in this patient varied from 9.9 to 11.10 mg. per 100 c.c.

In May, 1927, we gave the patient a series of parathormone injections totaling 200 units over a period of five days. At this time she had been bleeding continually for thirty-four days, using four pads a day. Her hemoglobin was 68 per cent Dare. She had been advised to have a vaginal hysterectomy for the bleeding by her previous physician. Two weeks later she passed through a normal menstrual period, using eighteen pads. When the patient was last seen, October, 1927, she had gained forty pounds and was menstruating regularly each month, using eight pads during a period which lasted three days.

CASE 3.—This patient, whom we also reported in our first series, had three periods of parathormone injections. During the first menstrual period the patient was given eighty units of parathormone on the first day of her menstrual period in two doses. She suffered from nausea, chills, vomiting, and severe headache. The temperature rose to 103.6 and pulse to 120. Blood calcium determined at this time showed only 10.52 mg. per 100 c.c. The temperature returned within two hours to normal, resembling a foreign protein reaction. The menstrual flow stopped for six hours and the period was shortened one day and by six pads. Forty units of the eighty used here were given intravenously and were followed by this marked reaction. During the next two periods smaller doses, but totaling eighty units, both subcutaneously and intravenously were given without reaction, however. We have not given any of the hormone intravenously since this time. The calcium variations were well within normal limits. Shortly after this the patient was married. We have had reports from her for a period of several months during which her periods were normal. She had not become pregnant.

CASE 4.—This patient was thirty-four years old. She had had a menorrhagia extending over a period of four years. This varied from a very profuse period during which she used three dozen pads in ten days to a constant flow lasting for a month or more at a time, during which she would use from one to two pads

a day. The patient had been curetted twice elsewhere without relief. The year previously she had been given a radium treatment, dosage not known. Following this she had an amenorrhea of one month followed by two relatively normal periods. Since that time she had been bleeding profusely as described.

The patient was given two series of parathormone injections. The first one, forty unit doses each day for four days accompanied by 150 grains of calcium carbonate by mouth each day. The blood calcium at the end of this period was 13.98. There was no reaction. Bleeding ceased entirely for ten days. Due to some oversight, when parathormone injections were begun again only twenty units were given each day. The patient continued to bleed and two weeks later an abdominal hysterectomy was performed. The pelvic organs were absolutely normal. Histologically the endometrium revealed possibly a few more than normal distended glandular spaces.

CASE 5.—Patient, aged twenty-one, began to menstruate at sixteen years and until three years ago had had normal periods. During the past two years she has menstruated two weeks out of each month, using about thirty-six pads. Pelvic examination revealed normal findings. This patient was given forty units of parathormone and ninety grains of calcium carbonate a day. The blood calcium varied from 9.96 to 15.5 per 100 c.c. Medication was stopped due to the high blood calcium. No untoward symptoms were noted. The menstrual period was about the same duration as usual but the number of pads was decreased by one-half.

The menstrual flow has gradually increased until the periods are almost as profuse as they were previously. Her family physician has been giving her milk injections during the past few months but we do not know with what results.

CASE 6.—This patient was thirty-three years old. She entered the hospital in May, 1924, complaining of menorrhagia of two months' duration. The periods had begun at fourteen and except for a period of menorrhagia occurring at the age of sixteen, the periods have been normal, although accompanied by a rather severe dysmenorrhea.

Vaginal examination at this time revealed the uterus in third degree retroversion. The cervix was dilated and a rather large amount of endometrial tissue removed, which on microscopic examination revealed the cystic-like spaces that seem to be associated with this type of bleeding. The uterus was brought into position by the Webster round ligament operation. The pelvis was otherwise normal. Seven weeks after this operation she began to bleed again and has been bleeding irregularly but profusely since that time.

She was given two series of parathormone, thirty units a day for a total of 150 units, plus 180 grains of calcium lactate per day. The blood calcium at the end of this time was 13.24, and the patient had stopped bleeding. The time and amount of this period were halved. During the second period at the end of 100 units the patient complained of some headache, nausea, and had a pulse of 100. We have not heard from her since this treatment was given.

CASE 7.—This patient was a Mexican girl, twenty-five years old. She began to menstruate at sixteen and had had a menorrhagia lasting from eight to nine days, using eighteen to twenty pads. She had been married for five years and had not conceived. During the last few months the menorrhagia had gradually increased until there was some blood loss practically every day. This condition had threatened the marital tie and demanded relief.

We gave this patient 160 units of parathormone along with 180 grains of calcium lactate a day. At the end of this time the blood calcium was 9.98 whereas it had been 10.34 before the treatment was started. There was no decrease in the bleeding, so the patient was advised to have a treatment with radium. Since the patient was presumably sterile and the bleeding was such an important equation in her

family affairs, we thought it best to make reasonably sure of our irradiation results. These results we hoped to obtain by direct effect on the endometrium. Fifty milligrams of radium were introduced into the uterine cavity to remain in twenty-four hours. We introduced a triangular sheet of one-sixteenth inch lead, slightly larger than the uterus through a colpotomy incision, placing it directly behind the uterus and between the radium and the ovaries. This was packed into place with a gauze pack which also held the uterus forward and far distant from the ovaries. When the radium was removed patient was given a whiff of ethylene, and the lead plate and packing also removed. The pelvis was entirely normal to inspection.

This patient had an amenorrhea of one month. She then began to menstruate normally, using eight to ten pads each period. The periods have occurred at twenty-six to twenty-eight day intervals for the last twelve months.

CASE 8.—This patient was twenty-five years old, married six years, and had had no pregnancies. She began to menstruate at fourteen and had always had a profuse flow. During the last year the periods which had lasted from eight to ten days with twenty to twenty-four pads, had grown closer together until the patient was spotting much of the time.

We gave this patient a long series of parathormone, twenty to forty units at a dose, adding calcium carbonate sixty grains three times a day. Treatment was discontinued only when bleeding stopped. These periods of relative amenorrhea lasted from three days to five weeks. The blood calcium varied from 9.97 to 12.37. The higher calcium levels coincided with the cessations in bleeding. This treatment lasted over a period of six months and since that time we have lost track of the patient.

CASE 9.—This was a patient who had always had profuse periods since the onset of menstruation at fifteen years of age. She is now twenty-four years old. During the last two years the menstrual flow has lasted from eight to twenty-one days. During this time she would use from two dozen to fifty menstrual pads. She had been given at various times, with indifferent results, the usual oxytocics, foreign protein injections, and had been curetted once. During a period of six months this patient entered the hospital twice for bleeding and general weakness. The blood count and hemoglobin at these times were approximately normal. She was given two courses of parathormone and calcium lactate without appreciable effect. Curettage was resorted to in order to control the bleeding. The pelvis was normal to palpation under gas anesthesia. The blood calcium ranged from 10.17 to 13.58 during the period of treatment. The uterine scrapings revealed very little if any change in the endometrium, although it appeared to be in the resting stage in spite of the bleeding. The return to normal after the curettages lasted from three to six months before the menorrhagia reappeared. During the past few months without any treatment the patient has returned to a normal menstrual flow lasting three to four days and using ten to twelve napkins.

CASE 10.—This patient was twenty-six years old. She had been married seven years, during which time she had had two spontaneous abortions at three months' term, the last one three years ago. She entered the hospital with a history similar to that of the two previous three months miscarriages, complaining of constant bleeding. The uterus was only slightly larger than normal, was soft and doughy. The cervix was dilated and the uterus curetted. No evidence of pregnancy was found, so the culdesac was opened and the pelvis inspected. Everything was found normal.

The patient had normal periods for several months but during the past year and a half has been bleeding from twelve days to two months at a time, using

one to two pads a day. We began parathormone injections, using forty units each day; also giving 180 grains of calcium lactate. This treatment was continued for six days. The bleeding stopped and during the six months that the patient remained under observation she had irregular periods appearing every three to five weeks, lasting three to four days, during which she used six to eight pads.

CASE 11.—A girl, aged fifteen years, who began to menstruate at thirteen years. During the first year the periods came only at five week intervals but lasted two weeks, using about forty pads. During the past year the patient has bled from three to three and one-half weeks, using about the same number of pads which are more thoroughly saturated. Fainting spells have followed menstruation twice during the last four months.

This patient entered the hospital in the mid-menstrual period for a basal metabolic rate determination, which revealed a −3. She remained in the hospital three days and was given 120 grains of calcium lactate by mouth each day, added to which were forty units of parathormone given intramuscularly. The afternoon of the third day after the parathormone had been given for two hours the patient developed a severe headache, nausea, and a pulse of 136. She was extremely pale. The blood calcium had risen from 11.72 to 14.52. The patient was dismissed from the hospital late that evening in good condition and since that time has had normal menstrual periods lasting from four to five days, during which she soils from twelve to fourteen napkins.

CASE 12.—This patient was also a girl of seventeen who had had very profuse periods since the onset of menstruation at fourteen. During the last year the periods had continued from ten days to two weeks at a time, during which twenty-four to thirty-six menstrual pads were used. She was given a series of five parathormone injections of forty units each. She was so nauseated during periods that she was unable to take any calcium. The hemoglobin at this time by the Newcomer method was 44 per cent. The blood calcium at the beginning of the treatment was 10.66, at the end 10.50. Basal metabolic reading was +11. The patient had two normal menstrual periods of three days duration, using ten to twelve pads. Following this she was married and left the city. We have not heard from her since.

CASE 13.—This patient was thirteen years of age. She began to menstruate at eleven years. The flow had been profuse from the onset, the first period lasting seven weeks. The periods have been quite irregular. She has been flowing steadily for the last three months, using one to two pads a day. The hemoglobin was 58 per cent. Vaginal examination was negative. On January 21, 1928 basal metabolic rate was −26. She was given thyroid, grain one-half, three times a day over several periods. Menorrhagia improved. On May 25, 1928 basal metabolic rate was +9; she had been bleeding for two weeks. She was given parathormone, forty units each day for four days. Bleeding stopped and did not reappear for three weeks. Bleeding reappeared and was so profuse that the uterus was curetted on August 3, 1928. Scrapings revealed an endometrium apparently normal.

CASE 14.—A young woman, nineteen years old, began to menstruate at fourteen. The longest interval between periods has been ten days. Most of the time it is only a spotting of blood, but the patient bleeds profusely at irregular intervals. She has been unable to finish her school work. Three years ago she was curetted with no relief. Endometrial specimens obtained at this time were quite normal. The basal metabolic rate was −13. In a period of two weeks on thyroid therapy the patient developed an increase in the pulse rate and nervousness, so medication was stopped. There was no effect on the bleeding. Hemoglobin was 65 per cent. We gave her two courses of parathormone, 200 units each, distributed over periods

of five days each. Calcium carbonate, 120 grains a day, was given with the first period and calcium lactate, grains 180, was given daily during the second period. The blood calcium during the first series increased from 10.99 to 12.11 and in the second series from 10.35 to 14.56. At this time the patient developed severe headache, nausea, and a pulse which ranged from 120 to 140. The bleeding stopped. We have not heard from this patient since the last treatment.

Definite conclusions are hard to draw from such a small group of patients but we feel that the following points are of interest:

1. We obtained good results in five patients, fair results in six and poor results in three cases of severe menorrhagia treated with hypodermic injections of parathormone.

2. The optimum dosage seemed to be about forty units intramuscularly, given each day over a period of five days.

3. Most effective results were obtained by combining this medication with 120 to 180 grains of calcium carbonate or lactate by mouth per day.

4. Calcium levels bordering on the hypercalcemic state were obtained only five times, and only by this combination.

5. Patients having this high blood calcium (13.24 to 15.5 mg. per 100 c.c. plasma) usually complained of some headache, nausea, and a rapid pulse. Bleeding ceased at these levels.

6. Intravenous injections of parathormone would seem to be contraindicated.

7. The same condition that causes the menorrhagia seems to predispose toward sterility.

8. Direct effect can be produced on the endometrium by radium and the ovaries protected by the insertion of a lead screen through the culdesac in patients where medication fails. We hope to be able to report additional resistant cases treated by this procedure in the near future.

We wish to express our thanks to Dr. N. Sproat Heaney for his help in this work.

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THE METABOLISM OF GALACTOSE

V. The Effect on the Tolerance of the Cycle of Reproduction

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IN A PREVIOUS paper* we have reported the results of studies on the influence of ovarian activity upon the assimilation limit of galactose. The phase dealing with the several stadia of the reproductive cycle was omitted, as the agencies then operative, severally determine special and unique factors in the carbohydrate metabolism. The present paper communicates the results of studies during this physiologic period, with such interpretations as the facts seem to warrant. The problem is twofold, for, as has been previously noted, changes in the level of ovarian activity in the main parallel the changes shown by the sugar tolerance, while in the special phase now to be considered a wholly new and supplementary mechanism is engendered whereby the mammary glands synthesize galactose and lactose and produce an excretion of the latter by the breasts.

That the endocrine and exocrine activities of the ovary are closely related and seemingly mutually interdependent, will be conceded by all, but the description of the actual mechanisms with the allocation to cause and effect of the several factors involved constitutes one of the fundamental problems of present day science.

Waiving discussion of the putative endocrine stimuli of the several steps, modern thought regards the mechanism terminating in menstruation as a pseudogravidity which comes to an end because the impregnated ovum is lacking to condition the progress and outcome of a true pregnancy.

Frank[1] and his coworkers, on the basis of the Long and Evans[2] rat technic, regard the genesis of these several steps to be implicit in the production of a single female sex hormone produced initially by the follicle and found in the follicular fluid, later secreted by the corpus luteum, and lastly, arising from the placenta if conception has taken place. They demonstrate a cyclic appearance in the circulating blood of this hormone by the production of estrus in the spayed rat when blood extracts are injected. The onset of menstruation they regard as conditioned by the retrogression of the yellow body and consequent failure to secrete hormone into the blood stream, a disappearance of the active principle antedating the menstrual onset by an hour or two. Novak[3] has stressed the possible inapplicability of the results of these

*See this Journal, **16**: 687, November, 1928.

interesting experiments directly to human menstrual experience, and his scepticism finds definite response in many others. Affirming the facts as stated above, he regards the causal factor as still undetermined but feels that the ovum from the previous ovulation may be an element. Yet others consider the maturing follicle as the active agent, and a large group consider the so-called interstitial cells to be the causal unit. Whether ovulation continues during pregnancy is not known. The persistence of the corpus luteum would be an argument against this.

As conception is possible even though there be no cyclic bleeding, it follows that ovulation may occur without menstruation, but equally, that the converse is apparently not true. The assumption so frequently made that the presence or absence of menstruation defines the level of functional activity of the ovary is only correct within certain definite limitations.

The second point, correlative to our thesis, is the consideration of lactation. Changes in the mammary glands are coincident with certain modifications in the level of activity of the ovaries and accessory portions of the reproductive mechanism. These coincidences have been most interestingly correlated by Halban.[4] Limiting the discussion to the periods comprehended in the present study, we find the fact of pregnancy producing a growth impulse which prior to parturition adds a secretory activity first of colostrum and in a few days postpartum of milk. Ultimately the latter function ceases and involution of the breasts occurs. During this period of secretory activity, as noted above, cells in the breasts assume the function of synthesizing galactose, presumably from the circulating glucose and subsequently condensing the two sugars to form lactose.

It is generally recognized that throughout the period of pregnancy abnormalities of the carbohydrate metabolism occur. The appearance of glucose in the urine during pregnancy has been frequently remarked and depending upon the degree of pessimism of the writer, has been interpreted as diabetes, renal glycosuria, or a physiologic relief. The appearance of lactose just before confinement and its continuance, as determined by the course of the lactation period, have also received attention. There is a fairly diffuse literature on the subject, but the reports are highly conflicting. Much of the older literature can be discarded as the chemical methods employed lack accuracy and sensitivity. In a few of the later reports the incidence of glycosuria during pregnancy varies from the four cases in 468 (<1 per cent) reported by Cameron[5] to the 10 per cent recorded by Hirschfeld.[6] As the question was highly pertinent to the present study, the incidence of reducing bodies in the urines of several groups of pregnant and postparturient women was studied. All urines were tested with Benedict's copper reagent and if positive were quantitated with the familiar solution of

the same author. The patients were drawn from the several services of the Robinson Memorial.* Group *A* were women reporting to the Prenatal Clinic. Only twenty-four-hour collections were tested, as only by so doing was it possible to eliminate with certainty the glycuretic effect of a meal. Group *B* were house cases admitted for confinement and studied during their stay. The urines were two-hour specimens obtained by catheterization. The sugar was quantitated, and in addition both the mucic acid and Barfoed's tests applied. Occasionally an osazone was formed and its nature determined. Group *C* was similar to *B* but composed of different persons. The *D* group were patients from the postnatal service and had already been studied as members of either *B* or *C*. Again, as they were not under supervision, only twenty-four-hour collections were examined. The results of this preliminary series of observations follow below.

TABLE I. MELITURIA PREPARTUM AND POSTPARTUM

GROUP	DESCRIPTION	NO. OF CASES	MELITURIA	
			NUMBER	PER CENT
A	During pregnancy 4th to 9th month	100	18	18
B	1 day before delivery	50	19	38
	3 days after delivery	50	50	100
	4 days after delivery	50	50	100
	10 days after delivery	50	46	92
C	14 days after delivery	50	41	82
D	6 months after delivery	50	40	80

Our figure for the incidence of glycosuria (prepartum) is significantly higher than those recorded in Table I. This is probably due to the fact that each case was examined on several different occasions (an average of over 7). On this basis 18 per cent showed glycosuria at some time during the pregnancy. Nearly 12 per cent, however, gave repeated tests, a figure in good agreement with that of Hirschfeld.

With confinement imminent, about one-third of the women showed lactose in the urine, while in the first few days following labor all of them had an appreciable lactosuria. The combined results with this group are given in Table II.

TABLE II. CHARACTER OF SUGAR

TIME OF COLLECTION	BENEDICT	MUCIC ACID	BARFOED	AVERAGE AMOUNT
1 day before delivery	+	+	0	–
3 days after delivery	+	+	0	0.86 gm.
4 days after delivery	+	+	0	0.77 gm.
10 days after delivery	+	+	0	0.26 gm.

It will be noted that in no case was glucose present in detectable amounts. The quantity of the sugar fell rapidly, and on the tenth

*The authors take pleasure in acknowledging their indebtedness to the staff of the institution.

day four of the women were sugar free. A still further drop is shown in the figures for the fourteenth day postpartum, but this latter condition remained practically unchanged after a lapse of six months. A few typical results with this last group are given in Table III.

TABLE III. CHARACTER OF SUGAR—SIX MONTHS POSTPARTUM

CASE	TIME AFTER DELIVERY	LACTATION	AMOUNT	SUGAR* MUCIC ACID	BARFOED
A	180 days	Nursing	0.46%	+	0
Bl	171 "	"	0.21%	+	0
Bo	153 "	No (64 days)		negative	
Br	176 "	Nursing	0.43%	+	0
Bu	154 "	No (92 days)	0.39%	+	0
Ca	176 "	Nursing	0.37%	+	0
Co	185 "	"	0.52%	+	0
Ho	166 "	"	0.10%	+	0
Hu	178 "	No (156 days)		trace	
Jo	176 "	Nursing	0.49%	+	0
Le	161 "	"	0.20%	+	0
Lo	176 "	"	0.36%	+	0
O	194 "	"	0.27%	+	0
P	176 "	No (92 days)	0.39%	+	0
S	176 "	Nursing	0.46%	+	0

*Several of the urines were tested and gave lactosazone.

The striking feature here is the persistence of lactosuria in two cases respectively 92 and 156 days after interrupting nursing. It is only fair to assume that both possibly had some abnormality of carbohydrate metabolism which found expression in this condition. The presence of milk in the breasts regrettably was not determined. The amounts of sugar are reported in percentages, as it was practically impossible to persuade the subjects to bring the full collected amount.

The results given above would seem amply to confirm the numerous other records of melituria as a possible or probable incident of the reproductive cycle. In the lactosurias, overproduction is one patent explanation, but a similar explanation cannot be offered for the glycosuria observed in midpregnancy. In the main, it may be said that there is general agreement on the point that pregnancy tends to produce a lowering of the sugar tolerance, although the degree and frequency of incidence vary widely among the individual investigators. Reports like that of Bauch,[7] who found no change in the galactose tolerance of pregnant women using a test meal of 40 grams, result from a failure to recognize the carbohydrate paradox.[8]

The numerous tests for the early determination of pregnancy, with modified carbohydrate tolerance as the basis, well express the trend of current thought even though all these procedures have been shown to be both positively and negatively misleading. That this should be so is not surprising when one considers that functional failure of the ovary always lowers sugar tolerance and may produce amenorrhea.

TABLE IV. PREGNANCY

	CASE NO.	AGE (YEARS)	PARA	MONTH	WEIGHT DEVIATION	ALVEOLAR CO_2 (MM.)	BASAL RATE DEVIATION	BLOOD SUGAR (MG.)	GALACTOSE TOLERANCE
A	B–297	29	ii	3	–19%	29	–23%	97	20
	B–299	37	i	3	+14%	34	– 3%	100	20
	S–531	34	iv	4	+ 4%	27	–13%	83	20
	B–33	35	ii	6	+13%	24	– 6%	94	20
B	An	30	i	6	+24%	32	+ 1%	84	30
	Pr	22	i	7	+43%	29	– 1%	76	30
	Gi	28	ii	7	+63%	30	+ 8%	81	30
	Su	21	ii	8	+21%	27	+ 1%	75	20
	Lu	31	ii	8	+35%	34	+11%	89	30
C	H.M. 4	14	i	5	+12%	30	– 9%	75	20
	H.M. 2	20	i	5	+ 5%	34	– 5%	79	20
	H.M. 5	14	i	5	– 4%	32	– 7%	84	20
	H.M. 7	17	i	5	–11%	38	– 7%	79	20
	H.M. 6	20	i	7	–12%	34	+18%	91	20
D	M–9	34	ii	0	+14%	45	–14%	100	40
	M–9	34	iii	2	+24%	35	– 7%	100	30
	M–9	35	iii	9	+32%	41	– 5%	91	20
	M–8	29	i	5	+13%	29	– 9%	100	30
	M–8	30	i	9	+26%	37	– 6%	100	20

The use of a single test susceptible to so many unrelated controlling influences for the definition of one of them, can yield but dubious results.

Following the general method outlined in the preceding paper, we have determined the sugar tolerance of a few pregnant women. The cases were drawn from four different sources, namely, the diagnostic service of the Evans Memorial (A), a few suitable cases from the Prenatal Clinic of the Robinson Memorial (B), from a small nursing home (C),* and two volunteers, one of whom was studied prior to conception, and both throughout the course of their pregnancies (D). The methods of the earlier studies were employed, namely, weight deviation calculated from both Dreyer[9] (trunk length), and West's[10] standards, alveolar carbon dioxide by the Fredericia apparatus,[11] blood sugar after Folin-Wu[12] and the basal rate by the closed circuit method (Benedict-Collins apparatus), and comparison with both the Harris-Benedict[13] and Aub-duBois[14] standards. The galactose tolerance was determined by the method already described by one of us.[15]

The results here are highly suggestive. In the first three groups, comprising fourteen cases, ten show the prepubertal level of 20 grams. The remaining four, who are positive with 30, are from the out-patient group who were the least controlled. All the house cases show the 20 gram level, and that seemingly irrespective of the month of pregnancy. The most informative cases are the two constituting group *D*. (Table IV.) The small number of the complete series counsels reserve in interpretation. It is safe to say, however, that pregnancy lowers tolerance and seemingly tends to produce an assimilation limit identical with that of the prepubertal years or produced by castration. The implication of this fact will be considered later.

The tolerance of a small group (10 cases) was determined two weeks postpartum. It was found impractical to carry out the regular routine, and so only the galactose test was performed. The detection with certainty of small amounts of galactose in the presence of appreciable quantities of lactose offers some little difficulty.

The urine was rendered neutral (on the acid side) to phenolphthalein as an indicator, and 25 c.c. were treated with 5 c.c. of a saturated neutral lead acetate solution. After the precipitate had settled, one drop of lead solution was added to be sure that the operation was complete. The filtrate from this, which gives a heavy white precipitate, with a carefully balanced Barfoed's solution, was next shaken for one minute with three grams of Lloyd's reagent and again filtered. From this second filtrate 5 c.c. were added to 5 c.c. of the Barfoed's solution and boiled for thirty seconds. A very slight white precipitate will appear when the reagent and urine are mixed, but it does not interfere with the characteristic indications of a positive copper test. Under the conditions as given, 0.1 per cent of galactose is detectable with certainty, and 2 per cent of lactose yields a negative result even with three minutes' boiling. The only precaution lies in the careful

*The authors express their thanks to Miss Dorothy Gallivan through whose courtesy these data are available.

TABLE V. SIX MONTHS POSTPARTUM

CASE	AGE (YEARS)	PARA	WEIGHT DEVIATION	ALVEOLAR CO_2 (MM.)	BASAL RATE DEVIATION	BLOOD SUGAR (MG.)	GALACTOSE TOLERANCE	
				Lactating				
McD	24	i	+12%	31	− 9%	109	30	
St	25	iv	− 0%	41	−13%	98	30	
Mel	27	v	+39%	38	− 3%	80	30	
Ve	29	ii	−14%	39	− 8%	94	30	
Ch	36	ii	+ 7%	31	−11%	105	40	
				Not Lactating				
Fr	22	i	−21%	31	− 8%	97	30	Stopped 7 days ago
Du	26	iv	−22%	39	−13%	92	30	
Jo	27	iii	+28%	38	− 5%	118	40	
Cos	28	ii	+15%	42	−11%	95	30	
McC	32	i	−11%	36	+ 2%	98	40	
An	33	iv	+25%	43	− 9%	94	40	
So	35	ii	− 7%	39	−13%	95	40	
Ma	38	ii	+10%	45	−10%	111	40	
Ke	40	x	+ 9%	37	− 9%	100	40	
Ho	41	iv	+49%	37	− 4%	84	20	Pregnant

TABLE VI. INTERRUPTED PREGNANCIES

Case		Lo	Le	Be	Ke	O'B	Dee	Gl	Dim
Age	(years)	15	21	26	28	32	33	34	38
Menstrual History	Onset	13	14	13	18	12	15	14	15
	Regular	reg.	irreg.	reg.	reg.	reg.	reg.	reg.	reg.
	Duration	5 days	5 days	5-8 days	7 days	2-3 days	3 days	3 days	2-3 days
Condition		S	M	M	M	M	M	M	M
Para		i	ii	iv	iv	ix	ii	iv	v
Previous Miscarriage		0	0	1	2	2	0	0	1
Abortion	Cause	Self-induced	Self-induced	Trauma	Spontaneous	Spontaneous	Spontaneous	Trauma	Spontaneous
	Month	2	2	4	3	4	3	3	3
Interval to Test		5 days	5 days	5 days	6 days	6 days	6 days	7 days	6 days
Weight Deviation		+11%	+8%	+43%	+13%	+19%	+4%	−2%	+1%
Alveolar CO_2	(mm.)	39	49	43	39	36	42	43	39
Basal Rate Deviation		−15%	−13%	−7%	−22%	+1%	−7%	−8%	−2%
Blood Sugar		86	92	94	98	91	95	97	118
Galactose Tolerance		30	20	40	20	30	20	30	30

adjustment of the neutrality (slightly acid) relations, as basic lead acetate will carry down sugar and the Barfoed solution is very sensitive to a slight excess of acid.

With but one exception the threshold had fallen to 10 grams. The fact is presented without other present comment than that the saturation of the mammary glands with galactose is undoubtedly a factor in producing this unique level. The lowest recorded level for early childhood and for otherwise normal adult castrates is 20 grams. In the present case some superimposed agency must be operative, and the explanation offered above is an obvious one.

In the first group one of the subjects has regained the normal adult tolerance although still lactating, while the remaining four are still 10 grams below the norm. In the nonlactating group, six, or two-thirds, are fully normalized, and but three exhibit a tolerance level 10 grams below. One of these, it will be noted, stopped but seven days before the test. The case of Ho is added to the group as she had again conceived within six months of her earlier confinement. Her tolerance has fallen to the level which our experience associates with the later stages of pregnancy.

The data in Table V are consistent with the general trend. The high degree of saturation which is a feature in the early postpartum days has resolved itself into a state of equilibrium, and with the cessation of the function the glands gradually resume a state of sexual rest with resumption of the normal tolerance.

Supplementary information should derive from the study of cases in which pregnancy has been interrupted before its normal termination. Through the courtesy of the surgical staff, to whom we express our grateful thanks, eight such cases have been made available for this study. The collated data are in Table VI.

Of the three cases at the lowest level, one (Le) was a case of self-induced abortion by unknown means, the other two (Ke and Dee) seemingly spontaneous miscarriages, "Dee," however, being distinctly toxic while "Ke" had a basal rate of –22 per cent, a frankly hypofunctional level. Three of the four patients showing a level of 30 grams (O'B, Gl and Dim) were spontaneous miscarriages, while the fourth (Lo) was a fifteen-year-old girl whose abortion was produced by an extended series of douches supplemented by some drug. The one case with a normal tolerance of 40 grams (Be) had miscarried her previous pregnancy in the fifth month and the present in the fourth. There is some evidence here to suggest that with a sudden interruption of the pregnancy, the organism fails to react rapidly from the general state induced by the initial condition. With the miscarriage cases, on the other hand, the cause is seemingly endogenous, and it is possible that in some of them the condition producing the miscarriage was a progressive one of some duration. Possibly in these cases before the ter-

mination of the pregnancy the organism had begun those recessive processes which ultimately produce a normal level after the expulsion of the fetus. The number of cases is so small as to counsel extreme caution in the interpretation of results, and the above suggestion is only tentative. It is recognized that a larger series might produce results which would render this interpretation wholly untenable.

DISCUSSION

In discussing the details of this phase of ovarian activity, it must be remembered that two related but fundamentally different mechanisms are operative. The first, the hormonal influence, will be discussed later. The second, mammary activity, demands consideration. The several interrelationships can be presented in tabular form.

TABLE VII. RELATIONSHIP OF MAMMARY STATUS TO SUGAR TOLERANCE

PHASE	SUGAR TOLERANCE	BREASTS
Prepubescence	Low	Undeveloped
Mature	High	Developed
Pubescence	Increase	Increase
Menopause	Decrease	Decrease
Castration	Decrease	Decrease
Pregnancy	Decrease	Increase
Lactation	Decrease	Increase
Menstruation	Decrease	Increase (?)

In the static phases we find direct relation between degree of development and sugar tolerance. Further, in a single case,* ablation of the breasts for cosmetic reasons (malignancy lowers sugar tolerance) lowered the tolerance to the prepubertal level from that of normal maturity.

In the next three conditions, which are unassociated with lactation, we find a definite parallel between mammary states and sugar tolerance, as has been noted in the previous paper.

In the last three an antithetical relationship obtains which requires further comment. During pregnancy there is mammary increase with progressively falling tolerance. This, presumably does not mean saturation of the glands with lactose, as the melituria already discussed derives from the presence of glucose. With parturition the urine sugar becomes lactose, which is uniformly present, and the tolerance two weeks postpartum is lower than the prepubertal or castrate level. Here we undoubtedly have overproduction, and correlatively, saturation of the gland with galactose. As lactation progresses the tolerance rises, and while a subnormal level may be recorded after weaning, equally normal levels are found while the breasts are still secreting. Patently here are two agencies at work, the minor gland saturation superimposing on the major influence which manifests itself through-

*Seen through the courtesy of Dr. R. B. Greenough, to whom the authors express their sincere appreciation.

out the various levels of ovarian activity. Support for this thesis is found in the results during menstruation—a false pregnancy—where a lowered tolerance is recorded in those whose resting tolerance approaches the normal level. Whether the mammary growth impulse recorded at this period is an associated or coincidental phenomenon, has yet to be determined.

It would seem, from the foregoing, that mammary change is not the primary factor determining the fluctuations of sugar tolerance (with the possible sole exception of the early lactation level). That it does play an important rôle secondary to one, or probably more, hormonic influences conditioned by the several phases of glandular activity, would seem to be equally demonstrable.

Turning to the hormonal factor, we find a number of facts for which no satisfactory formula has as yet been suggested. Frank's generalization is seemingly applicable to women in a state of sexual rest (with the exception of the time of the menstrual period) but is directly contradicted by the observations during the several phases of the active cycle of reproduction. Küstner has also observed a premenstrual glycosuria appearing at the time of maximum hormone concentration which, if correct, is directly contradictory. With the elimination of the follicular hormone, as defined by Frank, there remain two potential endocrine agencies, i.e., the interstitial cells and the corpus luteum. The former constitute the less productive line of approach, for devoid as they are of cyclic variation, these much discussed entities are always present except in the case of castration (and less certainly after the menopause). To endow them with causal powers is to connote a wide range of functional differences which at once presumes their influence to be secondary to some outside controlling agent. In other words, they too are seemingly eliminated from the picture as far as any primary influence is concerned. There remains then the corpus luteum which Frank envisages as no more than a link in the chain beginning with the follicle and ending with the placenta, determining his so-called gestational gland.

Our own studies, in their present form, fail completely to resolve the question. They deal with but one end-result of a wide variety of causes, many of which are so intrinsically concerned as to be, at the present time, insusceptible to experimental elimination. So far as these observations go, however, they may be felt to indicate the probable elimination of any primary participation of the so-called interstitial cells. It is true that these cells, derived from the atresia of immature follicles, may function prior to pubescence. Certainly they seem less important after this physiologic boundary has been passed.

The whole general question remains in an unresolved state. The present experiments, from the viewpoint of the authors, offer one very definite contradiction to the general theory of Frank, and, at the same

time, suggest an independent activity of the corpus luteum which may be a dominant factor in the several phases of sexual activity. It is doubtful if it is alone. Far more probably there are a number of agents at work each influencing a special phase or special phases of the complete sex progression. Even the interstitial cells may play a part, but if so, it is not demonstrably the dominant rôle assigned to them by one school of endocrine thought. The results of the study may be briefly summarized.

SUMMARY

1. The several stadia of sex development and activity seemingly influence the capacity of female to assimilate and utilize galactose.

2. Lowering of ovarian function, from whatever cause, produces a like change in the galactose tolerance.

3. Criteria are established for the normal galactose tolerance of the female during the several stadia of existence.

4. The mammary glands play a most important rôle in the determination of the assimilation limit, but one apparently secondary to hormonic agencies which seemingly are the primary regulators.

5. From changes in sugar tolerance, it may be inferred that pregnancy produces a physiologic hypo-ovarianism which persists for some time after parturition but ultimately disappears.

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TORSION OF THE FIBROMATOUS UTERUS*

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THE occurrence of torsion in the fibromatous uterus, often termed axial or axis torsion, is of sufficient rarity and the accidents accompanying this condition are of such gravity that it would seem wise to report even a single new case. Likewise, since a survey of the literature reveals no recent case reports from this continent, and since no exhaustive thesis on this subject has been found except in foreign journals, an attempt will be made herein to outline briefly the known facts and literature of this interesting condition and to append a sufficiently detailed bibliography hoping that this may stimulate others to report similar cases which have come under their observation.

Case Report.—Mrs. E. J. R., 58 years old, married 30 years, with no pregnancies, having had normal menstrual history with menopause seven years previously, was admitted May 13, 1926, suffering acutely from severe abdominal pain, nausea and vomiting of twenty-four hours duration. During the past two years she had had two or three similar attacks of less severity which had subsided spontaneously. Her family physician had noted the presence of fibroid tumors for several years and had advised operation which the patient refused.

The temperature was 100°, pulse 112, respirations 28. White blood count was 18,000 with 82 per cent polymorphs, urine negative, cardiorespiratory examination negative. The abdomen was markedly distended and tympanitic with the suggestion of slight degree of shifting dullness in the flanks. Palpation revealed moderate generalized sensitiveness and peritoneal reaction with an area of maximum tenderness and spasm in the left lower quadrant. In this region a mass could be felt which extended upward to a level three inches above the umbilicus. Bimanually this tumor seemed closely associated with the uterus and felt like a fibroid in consistency, but its size and smoothness of contour together with its position to the left of the midline resulted in the diagnosis of ovarian cyst with either a twisted pedicle or degeneration from some sudden circulatory disturbance.

The patient remained under observation for another twenty-four hours during which time the vomiting became less, her fluid depletion was partially overcome, and the bowel was emptied by irrigations. Her general condition was better with pulse 108, respirations 28, temperature 101.4°, and white blood count 24,000, polymorphs 90 per cent. However, more definite localization of pain over the mass along with the rise in temperature and blood count, gave clear indication for operative interference.

Operation.—Nitrous oxide-oxygen-ether anesthesia was given. Lower midline incision was made. Upon opening the peritoneal cavity about a liter of bloody fluid was found in the lower abdomen and pelvis. The intestines were distended, but no mechanical obstruction or adhesions were observed. The mass was identified as a large fibroid tumor not pedunculated but growing from the top of the fundus

*Read at a New York Obstetrical Society, October 9, 1928.

and closely associated with it. This mass had undergone a torsion on its long axis from left to right of slightly more than 180 degrees so that the left cornu had been drawn around and rested almost in the hollow of the sacrum. The fibroid and uterus had the bluish-black appearance of early gangrene while the adnexa were elongated, swollen to three or four times their usual size, and markedly cyanotic. The broad ligaments were distended with lymph and their veins dilated in some places to 1.5 cm. in diameter.

As there were no adhesions, the torsion of the entire mass including the uterus was easily reduced, after which it was discovered that the pedicle of this rotation had been in the region of the upper portion of the cervix. A complete hysterectomy was done using the remains of the broad ligaments for peritonealization, and pelvic

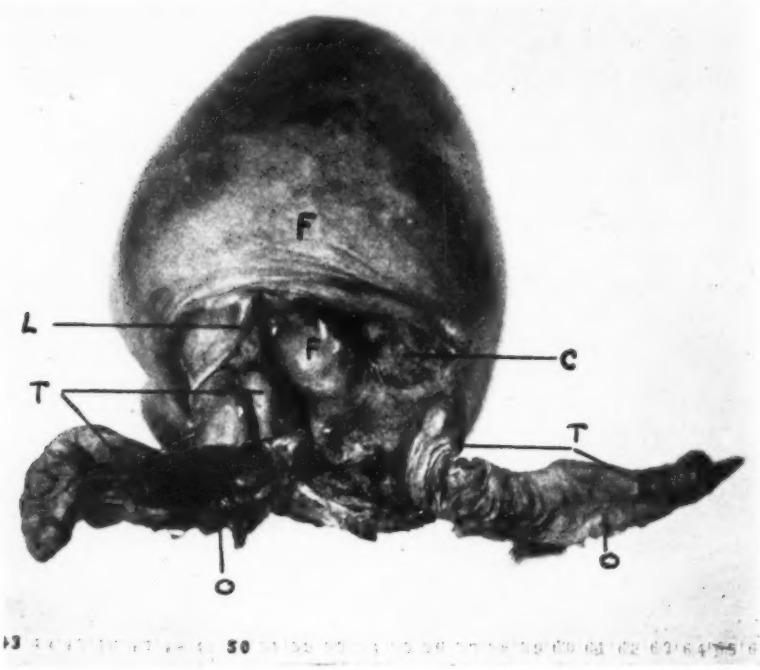

Fig. 1.—*C*, amputated cervix; *F*, fibroid; *L*, round ligament; *T*, tubes; *O*, ovaries.

drainage was established through the vagina. The abdominal wound was tightly closed without drainage. The postoperative course was uneventful, the patient leaving the hospital twenty-five days later.

Pathology.—The gross specimen (fibroids, uterus, tubes and ovaries) was 18 x 14 x 12 cm. in size and weighed 2600 grams. Its main bulk was made up of a single large oval smooth fibroid tumor, 12 cm. in diameter, which had developed from the top of the fundus posterior to the uterine cornua, and was attached by a broad base so that it was definitely sessile and not pedunculated. Anteriorly between the uterine attachments of the round ligaments were two small pedunculated fibroids about 3 cm. in diameter. The whole mass, including fundus tubes and ovaries had undergone early gangrene. On cross-section the tumor tissue was extremely edematous and contained many cystic spaces filled with lymph. Microscopically sections from every portion of the specimen showed all stages of degeneration from hyalinization to extensive hemorrhagic necrosis. The cervical canal was still patent and filled with mucus.

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The first case report of axis torsion seems to have been made by Times of England in 1861 in which he described torsion complicating a pregnancy. However, as the torsion seems to have been a minor factor in this observation most writers give credit for the first report of a true case of axis torsion in a fibromatous uterus to Virchow, who in 1863 described this complication in an autopsy on a woman sixty-two years old who had died of pneumonia. Since that date one finds in the foreign literature a gradually increasing number of case reports and from time to time an occasional detailed study in thesis form of this subject by a few careful observers.

No attempt will be made in the bibliography of the present paper to credit the author of each case report but the writers of the more important theses have as far as possible been included. Concerning the latter one may draw attention especially to the excellent observations of Schultze in 1898, Ferroni in 1899, Lepage and Mouchette in 1906, Girod in 1908, Piquand and Lemeland in 1909, Vautrin in 1910, Lhez in 1911, and Hitzanides in 1926.

An accurate estimate of the total reported cases of axis torsion of the fibromatous uterus is impossible without tracing out each individual report, as even in the exhaustive papers of approximately the same dates the estimated totals differ widely. These discrepancies may be explained by the fact that some authors exclude cases when pregnancy is an associated factor while others include all types of axis torsion. Piquand in 1909 collected 84 cases, 70 having occurred independent of and 14 associated with pregnancy. Hitzanides writing seventeen years later in 1926 reports a total of only 85 cases which apparently do not include any torsions associated with pregnancy.

Inasmuch as a brief survey of the literature at the present time reveals approximately 49 additional cases either not included in or reported since Piquand's original article one may assume that at least 133 cases of axis torsion of the fibromatous uterus have been reported to date. The reports of these additional cases have been carefully investigated to avoid duplication, and their salient facts are analyzed at the end of this article. They have been reported chronologically as follows by: 1904, Erdmann; 1905, Cameron; 1909, Connell, Fortun, Griffith, Jaschke, and Uteau and Baux; 1910, Olow (2 cases), Tehohaditch (2 cases), Vautrin (2 cases); 1911, Bland-Sutton, Jacobs, Lhez (2 cases), Meriel; 1912, Bucura, Dartigues, Kynoch, Secheyron; 1913, Poth; 1914, Ruppert; 1921, Dieulafe (2 cases), Malcolm, Vautrin (2 cases), Wigand; 1922, Whitehouse; 1923, Bernarbeig, Dambrine, Delepine; 1925, Dieulafe (2 cases), Jerlove, Lindig; 1926, Auvray, Didier, Enriquez and Boreo, Gordon-Watson, Hitzanides (2 cases), Massachu-

setts General Hospital Reports (Cabot's Clinic), Pouliquen, Walker; and 1927, Chauvenet. All of these cases are from the foreign literature except that of Erdmann and that shown at Cabot's Clinic in 1926.

ETIOLOGY

Age.—Axis torsion of the uterus occurs much more frequently in women over forty years of age. Piquand records 45 cases in which the age is known noting that 32 of these women were over forty years at the time of the torsion. In the additional 49 cases investigated in this article the age has been recorded in 41, of which 32 were over forty years. Naturally where torsion complicates pregnancy the age incidence is more often below forty but occasionally torsion not associated with pregnancy has also been noted in younger women. Such cases have been reported by Schultze and Löhlein at twenty-five years, Freund at twenty-one years, and the youngest case is noted by Woertz at nineteen years. The oldest cases are those of Bland-Sutton, Griffith, and Semmelink at seventy years.

Pregnancy.—Pregnancy does not seem to be an important etiologic factor in causing torsion in the fibromatous uterus. Of Piquand's 84 cases only 14 occurred in the gravid uterus, of which 11 occurred during the third and fourth month, 2 in the sixth month, and one in the seventh month of gestation. In no case is it recorded during the puerperium. Likewise the number of pregnancies seems to have only slight bearing upon the accident of axis torsion. Piquand has collected 44 cases with complete history, of which 12 were virgins, 8 in nulliparae, while 24 had had one or more children. Of these 24 there were 8 para-1, 6 para-2, 4 para-3, 2 para-4, 2 para-5, 1 para-6, and 1 para-7. Most authors agree that pregnancy by relaxing the abdominal wall and softening the uterine musculature may have some effect on the incidence of axis torsion but add that it is not one of the important predisposing causes. One notes that the literature of veterinary medicine reveals abundant examples particularly in the cow, of axis torsion of the uterus during pregnancy.

Size and Site of Development of the Tumor.—The size and weight of the tumor appear to have a direct effect upon the incidence of torsion of the uterus, as the great majority of cases reported show specimens weighing at least 2 kg. or more. Torsion has occurred in uteri containing tumors as small as 1.6 gm. (deGouillioud) and 1.7 gm. (Demantke), but these are rare, the average corresponding more nearly to that of Küstner which weighed 5 kg. Others have been reported as 7 kg. (Ivanoff), 13 pounds (Meridith), 10 kg. (Stratz), 11 kg. (Faure), and 15 kg. (Piccini). As the growing tumor approaches the average weight reported in these cases, it necessarily rises out of the pelvis into the abdominal cavity in which situation it may more easily twist upon its long axis. Likewise the upward traction force of the

rising tumor is exerted for the most part upon the uterine isthmus which is drawn out and much attenuated thus rendering it less resistant to torsion.

The situation and type of tumor also have a direct bearing upon torsion. These tumors are usually classed as pedunculated or sessile (interstitial) in type. The pedunculated tumors are situated most often away from the midline of the uterus, and torsion of their pedicles is less often transmitted to the uterus itself. This is not true if the pedicle happens to be attached near the midline of the fundus, for in this position the twist on the pedicle is more readily imparted to the fundus beneath it. Thus Piquand notes that in 22 cases where axis torsion of the uterus was caused by the twist of pedunculated fibroids, in 19 the pedicle was attached at or near the midline.

On the other hand the interstitial or sessile tumors are more likely to cause torsion if they are situated away from the midline near one or the other cornu. Here the leverage force of the eccentrically placed tumor seems to increase the likelihood of torsion. In 69 of Piquand's cases torsion resulted from the pedunculated fibroids in 32 and from interstitial fibroids in 37. A few cases have been noted of double torsion, that is, torsion of a pedunculated fibroid and a coexisting uterine torsion (Bantock, Johannowsky, Schwartz and Ferry).

Causes of Torsion.—A satisfactory explanation of the mechanism of torsion in either cysts or fibroids has not been evolved. Likewise in axis torsion of the uterus, while one can recognize certain predisposing factors, still the true exciting force responsible for initiating the rotation has never been clearly described.

As has already been stated, a tumor growing and increasing in weight, lying free in the abdominal cavity, if pedunculated and attached near the midline of the fundus or if sessile and placed eccentrically causing unequal weight to one side or another, and especially if the uterine isthmus has been stretched and thinned out by the upward pull—a tumor with such characteristics will unquestionably be more easily rotated, but the forces which cause this rotation are obscure.

Some authors stress the fact that the normal growing uterus of pregnancy is frequently somewhat dextrorotated and feel that the same conditions exist for the growing fibromatous uterus. Others (Piquand and Vautrin) point out that the right lumbosacral fossa is empty while the left is occupied by the sigmoid colon and rectum and attribute the tendency toward dextrorotation in the majority of cases to the fact that as the fibroid uterus rises it falls toward the empty right fossa and that such movement is encouraged by the repeated shocks of the peristaltic motion of the sigmoid in the left fossa. They add that this offers the best explanation for the dextrorotation in the slow or chronic

form of torsion and that, once initiated, the weight of the tumor and the resisting force of the abdominal wall will continue the rotation. In acute cases they feel the same conditions ensue but that the initiating force is more often some type of external violence or sudden muscular effort. The usual tendency toward dextrorotation may thus be suddenly increased; or, on the other hand, if the force acts in the opposite direction, this tendency may be so completely overcome as to result in a torsion from right to left. Once any given acute torsion is established, the intraperitoneal reaction will cause sufficient abdominal wall spasm to maintain it.

Then also if adnexal complications such as ovarian cyst or tubal inflammation exist, these may even be factors, especially if unilateral, which determine the direction of the rotation, particularly in the slow and more chronic form.

PATHOLOGY

In general the pathologic changes in the pedicle, the fibroid and uterus, the adnexae, and the surrounding organs are much the same whether these changes result from the acute or chronic form of torsion, the essential difference being only that of the degree of the circulatory involvement to the above parts.

The Pedicle.—Torsion occurs as a rule at the level of the elongated and thinned out isthmus. Stratz, Lannelongue and Vitrac have reported cases in which the torsion was produced with the uterine body as a pedicle, but such instances are rare exceptions. The direction of rotation is usually from left to right, and as has been stated the explanation of this phenomenon is not fully understood. Piquand notes that only 13 times in 84 cases has torsion been observed from right to left. The degree of torsion varies from 90 to 360 with a few exceptional cases reported by Micholitsch, by Wertheim, and by Homans of twists approximating a turn and a half, and others by Friedel-Pick, Schultze, Küstner, and Polak who found slightly more than two complete turns. As a rule, however, the restraining broad ligaments do not permit a rotation of more than 300 degrees, in fact the average case approximates 180 degrees. The obliteration of the uterine canal within the pedicle at the level of the isthmus varies somewhat with the degree of the torsion and the length of time that the twist has existed. In practically all instances at this point there is a mechanical blockage of sufficient tightness to prevent an attempt to pass a sound into the uterine cavity. In acute cases which are treated early, detorsion will leave the cervical canal normally patent. On the other hand in chronic cases obliteration due to pathologic changes within the pedicle itself vary from slight fibrosis to a complete severance of continuity, the upper cervix existing only as a thin fibrotic cord (Faure

and Vautrin). The extent of such an obliteration depends directly upon the length of time the torsion has existed and not upon the extreme degree of rotation.

The Fibroid.—In torsion cases the offending tumor, especially when pedunculated and often when sessile, is of the single variety though multiple smaller tumors may coexist. Extensive venous stasis with only partial arterial obliteration usually causes marked edema of the peritoneal covering of the tumor giving it a thickened, violaceous appearance bordering on early gangrene. The muscular and fibrous elements of the tumor are widely separated by lymphatic infiltration so that many cystic spaces form within it, the larger ones often containing a half liter of serous or serosanguineous exudate. These changes, while much more common in the acute torsions, do occur to a lesser degree even in the slow or chronic forms of rotation. In the latter, however, the establishment of collateral circulation often prevents extensive cystic degeneration. Advanced stages of gangrene rarely occur even in the acute form for the arterial supply is practically never completely destroyed.

The Uterus.—Changes within the uterus depend chiefly upon the age of the patient and upon the degree of obliteration of the uterine canal. In acute cases one finds only the circulatory changes within the muscle wall and mucosa, but in the chronic cases where rotation has been gradual and of long duration hematometra and even pyometra may result if the patient is within the menstrual age. In chronic elderly cases there are varying degrees of fibrosis of the uterine wall and often a fibrotic degeneration of the atrophied endometrium.

The Adnexa.—The tubes and ovaries are usually displaced, the left adnexa commonly resting behind the symphysis and the right one within the hollow of the sacrum. In acute torsions they are markedly swollen, often ecchymotic, and the tubes are frequently drawn out to twice their usual length. In chronic cases the ovaries undergo marked cystic degeneration with considerable surrounding peritoneal reaction causing sufficient exudate to gradually form very dense adhesions, while the tubes may become closed resulting in hemato- and hydrosalpinges.

The Bladder and Ureters.—As the growing tumor pulls the uterus upward into the abdominal cavity, the bladder is frequently greatly displaced, and torsion may result in considerable compression with edema of its walls. The ureters may be displaced and even obstructed (Dieulafe reports such a case complicated by hydronephrosis) but such accidents are extremely rare.

The Cardinal Vessels.—Torsion even in the region of the isthmus seldom completely obliterates the uterine arteries, for their fascial coverings are sufficiently independent of the cervical tissue that they

do not as a rule undergo the same degree of twist. Likewise the ovarian arteries in the infundibulopelvic ligaments are only partially blocked. The principal circulatory change is seen in the venous plexuses of the broad ligaments which are tremendously hypertrophied and surrounded by intraligamentary pools of serous exudate.

The Surrounding Structures.—The omentum, small and large intestine, and the parietal peritoneum are frequently involved in chronic cases. Dense adhesions gradually develop between these structures and the main mass of the tumor or adnexae, and occasionally considerable collateral circulation is set up through these new attachments, thus seriously complicating the operative procedure. The early establishment of these adhesions is regarded as the chief obstacle to a spontaneous detorsion.

SYMPTOMS AND SIGNS

The clinical symptoms noted in axis torsion of the uterus roughly fall into two groups depending upon whether the torsion is acute and sudden or slow and progressive.

In acute torsion the onset is sudden and severe, the patient frequently being affected during work or awakened at night without any prodromal manifestations. This suddenness of onset is comparable to that of ruptured ectopic pregnancy, the pedicle twists of ovarian cysts, or to strangulated hernia.

The pain in the lower abdomen is intense and soon becomes generalized producing pallor and at times syncope. The diaphragm is immobilized and breathing becomes rapid and shallow, while the pulse goes up to 110 or 130, the temperature in most cases remaining very little above normal. Reflexly vomiting and hiccough occur, and the former may vary from bilious to fecal in character. Usually in a few hours these symptoms become much less acute, and the patient remains comparatively calm. Later there may again be a gradual increase in the above symptoms with even some rise in temperature as absorption from the more or less gangrenous tissue ensues.

During the period of calm certain physical signs may be elicited which will aid in making a diagnosis. The fibroid tumor may usually be felt through the abdominal wall, and bimanual examination shows that it is closely associated with the uterus. Motion of this mass is extremely painful while the fornices and culdesac are empty and free of induration. The vaginal vault and cervix are usually pulled up to considerable height so that the examining finger may have difficulty in reaching them. The impossibility of passing a sound or catheter into the uterine cavity is a diagnostic sign of the utmost importance and has been stressed by all writers on this subject. In acute cases the patient's condition is so grave and the indication for operative interference is so clear that few surgeons will undertake such a diag-

nostic procedure; however, in the cases of chronic torsion this sign is of great value and should be employed if the diagnosis is to be verified.

In slow or chronic torsion the presence or absence of symptoms and signs depends upon the method in which this complication occurs. In general, chronic torsion is established either by a gradual and insidious rotation, clinically free of symptoms and often unsuspected before operation, or by a succession of more sudden twists resulting in subacute attacks with free intervals of varying length between. This latter type of chronic torsion often ends in a violent attack of the acute form. In fact from the histories obtained in most cases it is generally agreed that the latter syndrome is the one most commonly observed. The interval between such subacute crises is usually two or three months, and three or four years may elapse before the symptoms of an attack will be severe enough to bring the patient to the surgeon. During such a period of time other symptoms may develop from the adhesions formed to surrounding structures especially the intestines.

If the patient is within the menstrual age and the cervical canal is partially obstructed, disturbances of menstrual flow and dysmenorrhea may develop; or again, if the canal is blocked, the symptoms of hematometra or even pyometra may appear. It is in such cases that catheterization of the uterine cavity will give positive information in establishing a diagnosis.

Frequently the displacement of the bladder so alters its capacity and function that symptoms of urinary distress are noted. Here again both catheterization and x-ray will aid in recognizing such a displacement.

DIFFERENTIAL DIAGNOSIS

The diagnosis of axis torsion of the fibromatous uterus has seldom been made before operation. It is usually confused with twisted ovarian cyst or ectopic pregnancy and occasionally with adnexal disease, appendicitis, and intestinal obstruction. Differentiation between torsion of the uterus and of a cyst is most difficult as the physical symptoms and signs may be identical. Here again catheterization of the uterine cavity is a great aid in all cases while the suppression of menstruation may prove a valuable point in the younger women. On the other hand such amenorrhea has, in some instances, led to the diagnosis of uterine pregnancy. The presence of the large tumor with the point of maximum tenderness over it, rather than to one side or in the flank, along with the absence of signs of blood or exudate in the fornices and culdesac, aid in eliminating ectopic, salpingitis, or appendicitis. The gradual cessation of vomiting within a comparatively short period of time, along with the success of colonic irrigation and similar treatment will soon indicate the absence of a true intestinal obstruction.

Prognosis.—It is quite possible that some few cases of uterine torsion may undergo spontaneous reduction but such an outcome is exceedingly rare. On the other hand an occasional case of slow insidious torsion may through its adhesions develop sufficient collateral circulation to prevent gangrene, but at the same time these tumors often undergo fibrotic degeneration and eventually become calcified. Such instances have been reported by Vercoutre, Goullioud, and Ferrand.

For the most part, however, in all types of uterine torsion left untreated the prognosis is exceedingly grave due to the rapid development of circulatory complications. In Piquand's series of 84 cases, 8 were untreated and of these 6 died, a mortality of approximately 75 per cent.

On the other hand the prognosis after operative interference is much more favorable. In acute cases with early operation just after recovery from the initial shock of onset the mortality is practically that for ordinary fibroid hysterectomy in elderly women. However, any protracted delay of operation for a week or ten days greatly decreases the chances of a favorable outcome because of the extent of the gangrene, sepsis, and peritoneal involvement. In chronic cases without extensive adhesions operation offers comparatively little risk, but at times these torsions of long duration may necessitate extremely difficult dissection and the mortality in such instances is slightly higher.

Piquand reports 76 cases of fibromatous uterine torsion with operative interference, in 13 of which pregnancy coexisted. Of the 63 nonpregnant cases 7 died, and of the 13 pregnant cases only one ended fatally, thus giving 8 deaths in 76 operatives, or a mortality of 10.5 per cent. The marked difference in the results in the gravid and nongravid groups may be explained by the fact that the latter patients are for the most part well over fifty years of age. Barrozi reports 41 cases with an operative mortality of 7 per cent. Such figures markedly emphasize the seriousness of these uterine accidents, but when one compares them with the almost inevitable end-result if untreated, operative interference then becomes not only a matter of choice but of necessity.

TREATMENT

In a few instances (Rokitansky and Vercoutre) attempts have been made to manually reduce axis torsions of the uterus without operation but such efforts have seldom been successful. Such a procedure, even if possible, is strongly deprecated by all writers, for the chance of subsequent acute torsion is almost inevitable. The presence alone of the usually large fibroid in these patients warrants operation so that when axis torsion occurs such procedure may be said to be doubly indicated.

The type of operation employed varies with certain circumstances. Factors which influence the decision as to procedure are the age and

condition of the patient, the extent of the circulatory disturbance in the organs involved, and the presence or absence of an associated pregnancy. The most advantageous time for operation is generally conceded to be during the period of calm and improvement, which, in acute torsions, follows the shock of the initial onset; while in the more chronic and insidious twists operation is seldom imperative, in fact these forms of rotation are frequently unrecognized before laparotomy.

In young women with comparatively little tissue damage of the uterus and adnexae, myomectomy is the operation of choice, provided the tumor is pedunculated or, if subserous, easy of access. In these cases the uterus, relieved of its predisposing factor toward torsion, does not tend to rotate subsequently. However, if such an outcome is regarded likely it may be avoided by ligament suspension as advocated by Holst. Piquand notes 18 instances of myomectomy for uterine torsion caused by fibroids with no deaths. On the other hand even in young women the general state of the patient, the location of the tumor, and the damage to the uterus are often sufficient to demand hysterectomy.

In the acute torsions of elderly women and in the chronic torsions of all ages hysterectomy is usually done. Near or after the menopause indication for preserving the uterus no longer exists, while in the chronic cases the presence of organized adhesions around the tumor and uterus, as well as the chronic degenerative changes in the adnexae, make complete extirpation advisable.

In acute cases most operators prefer the subtotal or supravaginal hysterectomy, as these patients are usually gravely ill and such procedure offers an easy, rapid method of removal with the least possible additional trauma. After manual reduction of the torsion this operation is accomplished in the usual manner. In spite of the anatomic distortion the cardinal vessels are easily identified and their hemastasis offers no difficulty. Control of bleeding from the tremendously hypertrophied collateral venous plexuses within the broad ligaments may cause some concern, and careful ligation of these vessels well beyond the area of any thrombosis is strongly advised. Micheli reports one death from postoperative hemorrhage due to the loosening of a ligature on one of these broad ligament vessels. The cervix as a rule is markedly drawn out and thinned in the region of the isthmus and extirpation at this level is an easy matter. Total, or complete, hysterectomy may be done if the need of pelvic drainage warrants this additional procedure.

In chronic cases supravaginal or complete hysterectomy is recommended. While the general condition of these patients is less alarming, the operative procedure may often be more difficult due to organized adhesions, atypical collateral circulation, and coexisting adnexal complications. Here the advisability of complete removal of

the cervix depends upon the ease with which this may be accomplished, the necessity of drainage and upon the presence of cystic disease within its tissues.

Piquand reports 68 cases operated upon for axial torsion of the fibromatous uterus, of which 18 had myomectomy, 42 had supravaginal hysterectomy, and 8 had complete hysterectomy. In this series there were 60 recoveries and 8 deaths.

Treatment in Pregnancy.—In cases where axis torsion occurs in the pregnant fibroid uterus, the procedure varies with the age of the pregnancy. As this accident happens most frequently in the third and fourth months of gestation, laparotomy with careful myomectomy is usually practiced. According to Piquand 5 of such cases are reported by LePage, Thorn, Spaeth, Bland-Sutton, and Bourcart; in one of which (Thorn) a large subserous fibroid was removed, and in all five the pregnancy continued without interruption. When nearer term torsion may be of the slower variety and may permit of sufficient conservatism and delay to allow the patient to have a spontaneous labor; but, when more acute and the condition of both mother and baby demand interference, induction of labor with subsequent hysterectomy has been done, Dickinson some years ago having reported a successful case with such procedure. More recently, however, under similar conditions most writers agree that cesarean section with hysterectomy is the method of choice.

An anlaysis of the 49 case reports found in the literature since Piquand's complete article in 1909 follows:

The age was noted in 41, of which 32 were over and 9 under forty years. Obstetric history was given in 35, of which 23 had never conceived and 12 had had one or more children. Of the latter in only 3 cases did torsion occur during pregnancy. Menstrual history was mentioned in 37 showing that 15 had already had menopause and 22 were still menstruating, of which 10 experienced menorrhagia and 12 were free of any irregularity.

The size of the tumor was reported in 34, and in 32 the specimen weighed over 2 kg., the largest weighing 12 kg. The type of tumor was described in 39, of which 35 were sessile and 4 pedunculated; while in 31 the tumor was single and in 8 multiple. Reports were not sufficiently detailed to obtain accurate data on the site of implantation.

The direction of torsion was noted in 40, of which 32 were left to right and 8 right to left. In 39 the least degree of torsion was 45 and the greatest 450, with an average twist of 195. The patency of the cervical canal was indicated in 9 only, of which 5 showed blocking and 2 fibrotic obliteration while 2 remained patent. In 2 cases hematometra was encountered.

The type of case was recorded in 41, of which 30 were acute and 11 chronic. Of 33 cases the preoperative diagnosis was fibroid in 23.

ovarian cyst with twisted pedicle in 7, torsion of pedunculated fibroid in 1, while in only 2 cases was axis torsion suspected. Of the 40 operative procedures given, 34 had suprevaginal hysterectomy, 3 complete hysterectomy, and 3 myomectomy. The end-result was definitely stated in 41 cases, all of which recovered.

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(For discussion, see page 413.)

STERILITY, WITH SPECIAL REFERENCE TO THE SPERMATOZOON

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ONE of the most difficult and unsatisfactory classes of cases one is called upon to treat is sterility, where there is no obvious cause for the situation. The uterus is found to be in good position, there is no demonstrable pelvic pathology, and the menstrual history is normal. The husband's semen is examined and motile sperms are found, and yet, after several years, there have been no pregnancies. This class of cases is dealt with in the following paper.

It was formerly believed that the husband had been given sufficient attention if, or when it was found that his semen, usually brought to the office carefully kept warm in a thermos bottle or by some other arrangement, contained live spermatozoa in more or less goodly numbers. It is now beginning to be realized that a proper investigation of the possible responsibility of the husband in any given case of obscure sterility entails much more than this.

For some time I have been engaged in a study of spermatozoa, in an attempt to find answers to a number of questions which I never could find answered to my satisfaction, if at all, in textbooks on gynecology or urology, and only occasionally in a vague and general manner in special treatises on sterility. Among these are: What constitutes, morphologically, a normal human spermatozoon? How long should a normal sperm live, and how should its vitality be tested? What effect does the acidity of the vagina and acute and chronic infections, in both male and female, have on it? In cases of obvious poor quality of sperm, is the fault inherent in the spermatozoa, or have they been injured by their temporary habitat in "hostile secretions"?

While the material for this paper was being collected, two interesting articles have appeared, which give promise of furnishing some definite information regarding the possible answer in some cases of unfruitful marriages, in which both the husband and wife have been found apparently normal. Both of these articles have had to do with the male factor in the equation, and further reference will be made to them in this report.

The first specimens of semen and spermatozoa which were examined were from husbands of women who came because of failure to become pregnant, through marriages ranging from one and one-half to twelve years. Later specimens were examined which were obtained from men known to be fertile, having from three to five children. Some of these specimens were brought to the office in condoms, and some were ob-

tained by means of a pipette from the vaginal vault. For purposes of study of morphology, it made no difference.

Fig. 1 shows all the major differences in form which were found in all the specimens. There were innumerable finer variations in forms showing a difference in transverse diameter, ranging from that shown in "b," to that of "a," "g," or "i." These forms were observed and drawn as seen, several smears being made from each semen specimen, special care being taken in spreading, as it was found that rough handling broke many heads from the tails. I believe that this accounts for the forms "o" and "q," represented by Moench in his paper as being abnormal forms, since the one appears to be a normal head and the other a normal tail. As stated above, from the same semen specimen,

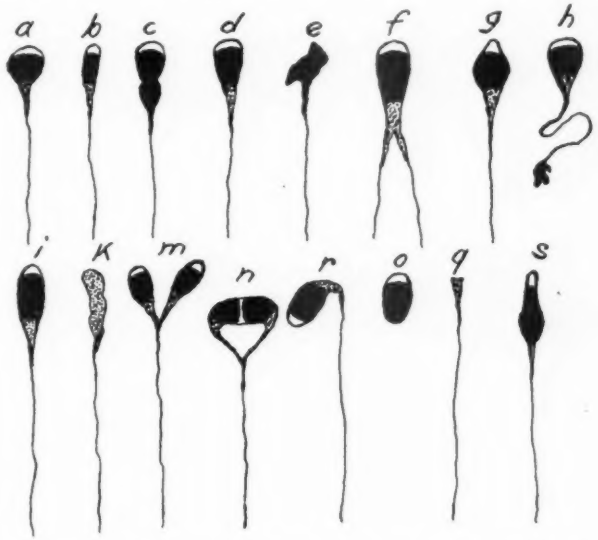

Fig. 1.—Tails shown relatively much shortened, except *h*.

it was possible to produce, on successive smears, an increasing number of these forms by increased rough manipulation of the smears in spreading. In the reported discussion of Moench's paper, Rubin voiced the belief that the double headed and double tailed forms were optical illusions or artefacts, and said that he had examined thousands of spermatozoa without ever having seen such forms. I agree absolutely with Moench that these are actual forms. In my own observations, I never saw the double headed forms except in two specimens, and in these two I always found them. All of these forms were seen in the unstained fluid preparations, and their movements studied, and were then examined minutely in stained preparations. Any good bistaining method suffices for satisfactory examination. A somewhat better smear is obtained if the mucus is removed from the slide before staining.

I am inclined to believe that forms such as "e" are artefacts, and caused by the flame in fixing. Forms such as "f," "h," "m" and "n" are not numerous; "r," in which the head is more or less sharply bent at the neck, is frequently common in certain specimens. The most frequent variation is in the lengths of the heads, and in their diameters. The structure of the spermatozoon is more complicated than is shown in the figures, especially the details in the connecting piece between the head and the tail. To show these, very high magnification and special staining methods are necessary, which are not feasible in routine clinical work, and which were not considered necessary for the purposes of this study.

In each specimen, from stained smears, with the high dry objective, and 10x eyepiece, 500 consecutive sperms were observed, and the number of grossly abnormal forms, without regard to type, were counted. The average of these forms in the specimens from sterile marriages was somewhat higher than those counted from specimens from husbands of fertile marriages, being 9 per cent and 5 per cent respectively.

The next step consisted in measurements of the lengths and diameters of the heads, and the lengths of the tails, of 250 consecutive sperms. The tail measurements showed nothing remarkable, as the ratio of tail length to head length ran pretty uniformly around 11:1. These measurements were made on forms adhering more or less closely to the recognized "normal" sperm, that is, those with elipsoid or ovoid heads, double headed or double tailed forms, as well as other "freak" forms, being omitted. It was found that some specimens showed a greater variation in lengths and diameters of the heads than others. When these microscopic data were correlated with the clinical data in the particular sterility problem being studied, it was found that the greatest variation occurred in the specimens from husbands whose wives showed the least cause for failure to conceive. This point will be discussed more in detail below.

The shortest head length found in any of the sperms measured was 2.5 microns, and the longest 8 microns. The shortest diameter was 1 micron, and the greatest 4.5 microns. These were combined to give heads shaped from almost or quite spherical to elipsoids with head length several times the diameter.

In all specimens, regardless of what percentage of grossly abnormal forms was present, or how much variation was shown in measurements of the remaining forms, the definite majority was always 5×3 microns in size, and of regular contour, as "i" in Fig. 1, with tails approximately 55 microns long, the heads being almost filled with dense nuclear material, except for an area of cytoplasm from 1.5 to 2 microns at the proximal end. This, I believe, may be taken as the gross morphology of the normal human spermatozoon, and I would apply the terms megalosperm and microsperm to forms larger or smaller than this, re-

spectively. This description is of the appearance "on the flat," in which position they are almost without exception viewed in stained smears. When on edge, they appear as shown by "s," Fig. 1, and this view is obtained readily only when they are observed in motion, with the high power, dry objective. Little variation was ever noted in this plane, but as none was observed so lying in stained smears, no definite measurements were possible. As indicated, variations in size of forms conforming more or less closely to this type are regularly found, the range of variation being greater in some specimens than in others. In many sperms, the nuclear material was stained much lighter than others in the same smear, the sperms otherwise appearing alike. This must represent some difference, but what it may be, I do not know.

Efforts to determine the vitality of the different specimens were now made. At first the patients were instructed to bring the specimens to the office with great care in regard to temperature, the condom being kept in the clothing near the skin, or in a thermos bottle at body temperature. It was soon found that such "hot-house" methods were not necessary. Specimens of sperms were repeatedly kept alive in a test tube, at room temperature, with no precautions except to provide against evaporation, for periods varying from twenty-four to sixty hours. Some specimens showed only a few or no live forms upon arrival, at periods varying from one to three hours after ejaculation. Thinking that perhaps some material in the condoms might be responsible for this condition, the specimens were poured out, and known normal specimens substituted. There was no apparent effect upon these latter specimens. Later, the semen specimens which showed all, or nearly all the sperms dead upon arrival in condoms, were almost invariably found to be in the same condition when removed from the vaginal vault, within the same periods of time after coitus. This would seem to absolve the vaginal vault and its secretions from fault in these cases.

As a result of observations upon the lengths of time that various sperm specimens lived, it was concluded that, roughly, normal sperms will survive in appreciable numbers for at least twenty-fours, under ordinary conditions of temperature, and that to obtain an estimate of sperm vitality, sufficient for clinical purposes, it is not necessary to keep the specimen at a temperature corresponding to that of the body.

By means of a stop watch, the time was measured which was necessary for fresh normal sperms to travel across known distances calibrated on the microscope eyepiece, and the average speed for 250 was found to be approximately 1.8 mm. per minute or about 11 cm. an hour.

Of course, too much importance is not to be attached to such a measurement of motility, since only those forms which swim in a straight line for a sufficient distance can be so measured, and it is evident that the distance which any sperm travels to reach the tube is more than the

actual distance from external os to tube. Also the motility of the sperms diminishes with increase of time after ejaculation. But allowing for these factors, it seems that a minimum of three or four hours is more than ample time for an appreciable number of sperms to reach their destination in the tubes.

Another observation was made in this connection, viz., that when portions of vaginal secretion were added to semen, an immediate stimulation was noted, whereby the motility of the sperms was definitely increased. This stimulation is only transient, and when left in an acid medium, their ultimate lives are shortened, usually by several hours, compared to the controls. This point has a significance which is discussed more in detail below.

Small amounts of semen from specimens containing virile sperms were mixed with much larger amounts of semen in which all, or nearly all, the sperms were found dead. The sperms remained alive as long in these mixtures as in the control tubes of unmixed semen. This would lead one to suspect that some defect inherent in the sperms themselves was responsible for their failure to live, and not some "hostility" of the prostatic or seminal fluids, as is so often given as a cause. If, as seems probable, the morphology of the sperms is an index to their fertility, it would appear reasonable to presume that the same influence which was responsible for the variation in morphology was also responsible for their diminished fertility, or lack of it. The sperms are formed in the testicle, and we cannot conceive that their temporary habitat in secretions of whatever character, before ejaculation, could alter their morphology, making some larger and some smaller, some with two heads or two tails, etc. As normal sperms die, there is no change in their visible forms, whether their motility ceases as a result of age in normal semen, or whether it is caused by chemical or physical agents inimical to their existence.

The factors which so influence the testicle to produce sperms with wide variation in morphology, vitality, and fertility, are unknown. This, of course, constitutes the ultimate problem, as our work is directed to treatment. Much has been said and done recently about diet in this connection. It seems to me that this could be a factor only in the very rare case. At present, at least in this country, our diets are varied enough to contain, presumably, all the vitamines necessary to our well-being. Diet has been well proved to be a factor in fertility and sterility, but the work has been done with chosen and controlled diets, in the laboratory, on animals. Under the same regulated conditions, rickets, beri-beri and scurvy can be produced. Clinically, in adults we see such cases as rarities, and when they are seen, they are far from being in the apparent good health in which we see most of the men and women who come to us because they have no children.

Certain it is that infection of the posterior urethra, prostate and seminal vesicles is not necessarily a bar to male fertility, since we see all too frequently the combination of a first pregnancy and an early female gonorrhea. In this series of experiments, the semen specimen which contained living sperms the longest (over sixty hours), under conditions described above, was from a man who had had gonorrhea eleven years ago, with unilateral epididymitis, and who now shows pus and much mucus in his semen, and who has a chronically inflamed prostate and vesicles. In another case, in which the couple have been married for five years, there is one child four years of age. Since the birth of this child there have been numerous pregnancies ending in spontaneous abortions at periods varying from two to four months. The Wassermann reaction is negative in both man and woman. Examination reveals an enlarged and tender tube on the left side, a badly lacerated cervix, probably dating from the birth of the first child, with a severe chronic infection (gonorrheal) of the cervix, with a profuse mucopurulent discharge. From her history, all of these symptoms, and presumably all of the signs, have been present for over three years. Examination of the husband showed a chronic gonorrhea, with enlarged and boggy prostate, and indurated vesicles on both sides. Obviously there is sufficient trouble here to explain the repeated abortions, but the point I wish to emphasize is that it has not prevented frequent conceptions.

As the semen specimens were examined from time to time, to determine the longevity of the sperms, it was observed that by far the largest percentage of the longest living forms was of those grossly abnormal, and this was much greater than the percentage of those forms present in the smear. Thus in one specimen containing 10 per cent of grossly abnormal forms, at the end of forty-two hours only five sperms were found alive. Of these only three were making progress; two of these were double tailed and one double headed. Both of the other two were megalosperms; they were moving, but making no progress. It would appear that, other factors being equal, those forms having the greatest amount of protoplasm tend to survive longer than those smaller, containing less. If this observation holds in a sufficiently large number of cases, one would be led to believe that it might be an explanation of the observation made by Williams and Savage in cattle, that abortions were more frequent in cows which had been impregnated by bulls whose semen contained a large percentage of abnormal sperms. If these forms are more virile, in a semen generally below par, the chances of such sperms reaching an ovum would be greater, resulting possibly in an abnormal embryo unable to reach maturity. The same may apply to cases of so-called habitual abortions in women.

It was at about this time in my own work that Moench's paper, based in turn upon the work of Williams and Savage on bulls, came to my

attention. This paper contained graphs of sperm head lengths, with possible prognostic value based on such graphs. In a few words, the graphs are obtained by plotting sperm head lengths along the abscissa, and the total number of each length along the ordinate. The graph will therefore be wider at the bottom in cases showing greater variations in sperm head length. Two of these graphs, modeled after those of Moench, are shown in Fig. 2. The first, *A*, shows much less variation than the second, *B*. The first would therefore be considered a much more favorable sperm specimen than the second. The wives in these two cases were studied carefully, and were found to be apparently normal, with the exception that each had quite heavy and tenacious mucus in the cervix, which was thought to be a factor in their inability to become pregnant. Uterine insemination was done in both cases, the semen being injected from the vaginal vault by means of a sterile glass pipette. The wife in the first case missed her next menstrual period,

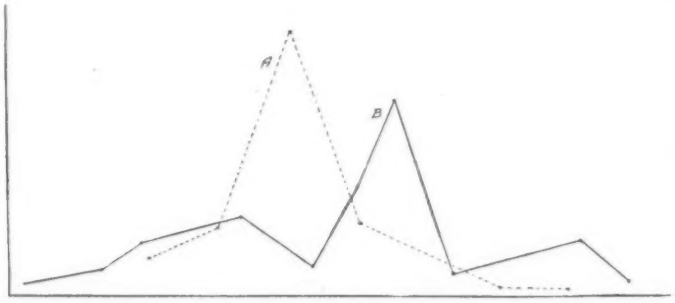

Fig. 2.—Sperm head lengths in microns along horizontal (3x actual for sake of emphasis), and total number of each length along the vertical.

Graphs are not superimposed, since the apex of *A* represents the same sperm head length as the apex of *B*, viz., 5 microns.

and is now normally pregnant. In the second case, nothing has happened, although three inseminations have been done. If such graphs are significant, they will prove a distinct help in fixing possible responsbility in doubtful cases of sterility, and in prognosis. As Moench states, hundreds of cases will have to be studied along this line before any definite rules can be formulated.

Kurzrok and Miller seem to have conclusively demonstrated a ferment or lysin in semen which is specific for cervical mucus. It is apparently absent in some semina. This is an interesting line of investigation, and could well explain some hitherto baffling cases of sterility.

I have been impressed, when removing specimens of semen from the vaginal vault, with the concentration of the sperms in the external os. It seems to be always greater here than in other parts of the vagina, in the "seminal pool," for example. This observation led to a series of experiments wherein a drop of fresh semen was placed in contact with a drop of vaginal material upon a slide, and observed under the micro-

scope. An increased motility of the sperms was noted in the region of the junction of the two drops, as was mentioned above when semen was mixed with vaginal secretion, but in a relatively short time (about ten minutes) all the more active sperms had moved away from the junction to the more alkaline portions of the semen drop. A very few had penetrated into the vaginal droplet, and a few feebly moving ones were found in the region of the junction of the two.

Now, clinically, the semen is always alkaline, the cervical secretion is uniformly alkaline, but the mixture of material found in the vagina and vaginal vault is acid. Positive and negative chemotropism is offered frequently as an explanation of facts observed in plant and animal ecology, and the same thing seems to play a part here. This change in reaction from the vagina to the cervix may serve to direct the sperms to and into the internal os, making the entrance to the canal not so much of a hit or miss affair as one might suppose from watching the multiplicity of directions taken by the sperms observed under the microscope.

The frequent direction to patients, therefore, who complain of sterility, and whose vaginal secretions are found to be acid, to take an alkaline douche just before intercourse, may serve only to place another obstacle in nature's pathway. I have not yet found a vaginal secretion so acid that, when mixed with semen in proportions far greater than those obtaining after intercourse, when dilution by the alkaline semen and increased alkaline cervical secretion has taken place, had any immediate effect upon spermatozoa except to stimulate their motility. Especially in dispensary practice, one is struck by the large number of patients who come for two things; some treatment to stop a profuse cervical discharge, dependent upon a chronic cervicitis, and which is always acid in the vagina, and contraceptive advice. In other words, these patients have a profuse acid vaginal discharge, and they do not complain of sterility. I have not yet found any evidence that there is an "aspiration action" of the human cervix, which is sometimes advanced to explain the entrance of semen into the uterus.

In another series of experiments, semen was placed in conjunction with, and mixed with, specimens of thick cervical mucus, obtained in each case from patients whose complaint was sterility. In no instance did a spermatozoon ever progress farther than a few microns into it. Many of them stuck to the edges of these masses, and were unable to move in any direction, although the movement of the tails was vigorous. These tests were made both with the husband's semen, and with known normal semen.

As a result of these observations, it was concluded that, in those cases where husband and wife are apparently normal, but where conception does not occur, and especially after careful examination of the semen shows it to be up to a normal standard of fertility, that the chief

bar to conception lies in the inability, for one cause or another, of the sperms to pass the barrier of the cervical canal and internal os.

The treatment therefore (and this is not new) is the introduction of the sperms into the uterus by means of a pipette. Needless to say, there should be no pathogenic organisms in the cervix or vault. In doubtful cases, condom specimens of semen may be used. Otherwise the patient is instructed to come to the office as soon after intercourse as possible, but not longer than an hour, when the injection is made directly from the vaginal vault. The injection of such material into the uterus is not without its theoretical dangers, but as yet we have had no accidents. Not more than a few drops of semen or material should be injected, and this gently; it is not the purpose to force it into the tubes, but to deposit it in the uterus. This treatment would also be indicated in those cases seemingly found by Kurzrok and Miller, in which a cervical mucus lysin is absent in the semen.

Here we are confronted again with the much debated question as to when ovulation occurs. Different authorities have placed it from nine to twenty-one days after the beginning of the last menstrual period. Loewe has published an article dealing with the recovery of the female sex hormone from urine, which shows that this hormone, while present to some extent all the time, appears in greatest concentration in the urine eleven days postmenstruation. Gustavson, who with Frank has done much work with the female sex hormone and its extraction, now uses urine exclusively as a source of hormone, since the absence of lipoids, etc., facilitates extraction and the hormone is obtained in more concentrated state than when obtained from the ovary or blood. The urine, then, is evidently a more accurate and sensitive indicator, so to speak, of changes in amount or concentration of this hormone in the body than other available fluids. Since the greatest concentration appears at the eleventh day, ovulation probably occurs then, or possibly shortly before this time. We have used the twelfth day for the first insemination, and if one is unsuccessful, the time may be varied a day or so either way the following month or months.

Naturally, the number of cases which meet the requirements for selection such as outlined will be small. Usually some grosser reason can be found for the sterility. So far, in my own cases falling in the former class, pregnancy has followed insemination in two cases, of two and six years sterility, and has failed in two others after three trials. In one of the latter, failure was predicted because of the failure of the sperms to meet requirements, and the second seemed to be a fair specimen when measured by standards as described above.

Last, but not least, we have assumed that a woman in good general health, whose menstrual history is normal, and whose genital organs show nothing grossly abnormal, secretes normal ova. That this assumption is correct in all cases is doubtful. At present we have no

means of knowing this except when conception occurs. As in other fields, we know very little about the delicate physicochemical reactions and balances concerned in the reproductive processes, and until more of the biologic fundamentals are known, our efforts in many obscure cases of sterility will be gropings in the darkness.

CONCLUSIONS

In some cases of sterility, no apparent abnormality, either in husband or wife, can be found.

Examination of the semen, in obscure cases, should be more exhaustive than is usually made. The percentage of abnormal sperms found in a specimen of semen seems to be an index of the fertility of the individual, and its determination offers an aid in prognosis.

It is possible that too much importance has been ascribed to so-called hostile secretions in the male genital tract in their influence on the sperms.

The acidity of the vagina seems to play a part in directing the sperms into the external os.

Thick tenaceous mucus in the cervical canal offers an effective barrier to the passage of sperms. The cervix and internal os offer the first, and probably the greatest, obstacle to the passage of the sperms to their place of union with the ovum in the tube.

Good general health and a normal menstrual history may not necessarily be assurance of normal ova.

Deposition of the sperms in the uterus by means of a pipette circumvents the barrier of the cervix and internal os, and in selected cases and with proper care in technic seems to be reasonably free from danger.

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THE RATIO OF UREA NITROGEN TO TOTAL NONPROTEIN NITROGEN IN THE BLOOD IN NORMAL PREGNANCY

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IN MOST samples of normal blood about 50 per cent of the total nonprotein nitrogen is accounted for by the urea nitrogen, although variations of from 35 to 55 per cent have been recorded.[1]

During the past decade there have been published the reports of numerous investigations dealing with the chemistry of the blood in pregnancy and incidentally with the problem of the relative concentrations of urea and of nonprotein nitrogen in this condition. The results of these investigations are practically unanimous in the findings regarding the low absolute concentrations of nonprotein nitrogen and of urea in the blood in normal pregnancy and also in the majority of cases of abnormal conditions. But the observations regarding the relative concentrations of these fractions are rather diverse. Thus certain investigators have found that the ratio of urea nitrogen to nonprotein nitrogen in the blood of normal pregnant women is much smaller than in the blood of the nonpregnant individual;[2] others have found this abnormality only in the blood in eclampsia and other pathologic conditions,[3] while on the other hand the results of several investigations are available which would indicate that this ratio is the same in pregnant and in nonpregnant subjects.[4] The lowered ratio of urea nitrogen to nonprotein nitrogen of the blood in pregnant women (if it exists) is of considerable interest both from the theoretical and from the practical side. The relation of the liver to urea formation has long been stressed by physiologists, while the occurrence of pathologic changes in this organ has been noted at autopsy in a sufficient number of cases of eclampsia to warrant the view that in certain pathologic cases at least, the damage to the liver may be sufficiently severe to give rise to an abnormal concentration of some of the constituents of the blood and perhaps even the urine. On the other hand it is difficult to account for the fact that in normal pregnancies the ratio of urea nitrogen to nonprotein nitrogen should be lower than in the case of nonpregnant individuals. Two theories may be mentioned, the first of which, advanced some years ago by Folin,[1] suggests that the pregnant organism may be extremely susceptible to the toxic effects of certain waste products and in self-defense may be compelled to keep these waste products at a sub-

*Dr. Denis died on January 10, 1929. In her death, scientific medicine, especially in the field of biochemistry, sustained a great loss. (E. L. K.)

normal level; the second that in order to nourish the fetus properly the maternal blood must contain a relatively higher proportion of amino acids and polypeptids than does that of the nonpregnant individual.

In view of the diversity of results which have been obtained by the earlier investigators it has seemed worth while to carry on a relatively extensive series of observations on the ratio of urea nitrogen to total nonprotein nitrogen in women at different stages of pregnancy and also for the first two months postpartum.

In a few cases we have been able to obtain a series of samples of blood from the same women taken at intervals during all or a considerable portion of the period of gestation.

In order to check our analytic methods we have also included in each series of 10 to 15 samples of blood taken from pregnant subjects the blood of one nonpregnant individual either male or female.

TABLE I. UREA NITROGEN, NONPROTEIN NITROGEN AND RATIO OF THE SAME IN 239 SPECIMENS OF BLOOD FROM 162 NORMAL PREGNANT WOMEN

MONTHS PREGNANT	NUMBER OF CASES	NONPROTEIN NITROGEN MG. PER 100 C.C. BLOOD			UREA NITROGEN MG. PER 100 C.C. BLOOD			RATIO UREA NITROGEN TO NONPROTEIN NITROGEN PER CENT		
		MAXIMUM	MINIMUM	AVERAGE	MAXIMUM	MINIMUM	AVERAGE	MAXIMUM	MINIMUM	AVERAGE
1	1			24.0			10.0			41.7
2	5	27.2	20.7	23.3	10.4	6.1	8.3	43.5	29.6	35.5
3	9	24.6	19.0	21.8	9.9	5.9	7.5	40.6	25.0	34.3
4	16	26.2	17.5	23.2	8.9	5.0	8.1	42.0	26.0	34.3
5	24	26.0	19.3	22.0	10.0	4.7	7.3	43.5	25.0	33.0
6	31	26.1	18.2	22.3	13.0	5.1	7.4	52.0	22.2	33.4
7	52	27.2	16.7	21.3	11.0	5.0	7.5	45.5	24.2	33.0
8	49	28.5	17.5	21.8	11.7	4.7	6.8	49.5	23.9	32.8
9	47	27.3	17.1	22.1	12.5	4.9	7.2	46.0	22.6	32.6

Our determinations of urea and of nonprotein nitrogen were made by the methods of Folin and Wu.[5] During the course of the investigation frequent check analyses were run on urea solutions of known concentrations, and during the latter part of the work check analyses were also made by the recently published manometric method of van Slyke.[6]

Our clinical material was obtained from the colored out-patient clinic and colored obstetric wards of the New Orleans Charity Hospital. The samples of blood were all obtained at about the same time in the morning and were brought immediately to the laboratory and analysed at once.

Our observations have extended over a series of 316 samples of blood taken from 162 normal pregnant women from the first to the ninth month of gestation, 55 samples of blood taken from 55 women from eleven hours to five months after delivery, and (as a check on our analytic technic) 14 samples of blood from 14 nonpregnant individuals. The ages of our subjects varied from fourteen to thirty-seven years,

TABLE II. UREA NITROGEN, NONPROTEIN NITROGEN, AND RATIO OF THE SAME IN 55 POSTPARTUM CASES

TIME ATER DELIVERY (DAYS)	NUMBER OF CASES	NONPROTEIN NITROGEN MG. PER 100 C.C. BLOOD			UREA NITROGEN MG. PER 100 C.C. BLOOD			RATIO UREA TO NONPROTEIN NITROGEN PER CENT		
		MAXIMUM	MINIMUM	AVERAGE	MAXIMUM	MINIMUM	AVERAGE	MAXIMUM	MINIMUM	AVERAGE
0.5	1			21.8			6.1			27.9
1	2	31.6	24.5	30.8	9.1	8.0	8.6	32.6	27.9	30.2
2	4	27.9	19.7	24.2	12.2	7.9	9.9	43.5	39.2	40.7
3	4	21.4	20.6	20.8	8.4	6.7	7.7	41.0	32.3	37.4
4	4	30.0	19.8	25.4	12.2	7.5	9.7	48.0	33.6	38.4
5	7	28.6	20.7	23.9	10.6	7.5	8.6	41.1	34.6	39.2
6	1			20.0			6.9			34.5
7	1			24.0			8.5			35.4
8	1			20.4			9.0			44.0
9	1			28.6			13.2			46.0
17	1			22.2			8.3			37.4
21	2	32.4	31.6	32.0	16.6	11.5	14.1	51.1	36.4	43.8
30	9	29.7	23.1	26.3	14.2	9.4	10.9	47.5	34.0	41.6
35	2	27.1	23.8	25.5	11.8	11.5	11.7	43.0	41.5	42.3
42	2	23.8	18.5	21.2	10.5	7.7	9.1	44.3	41.5	42.9
49	2	28.6	25.3	27.0	11.3	9.9	10.6	39.8	39.0	39.4
60	3	26.1	23.7	24.9	11.3	10.5	10.9	42.3	40.2	41.3
90	3	30.4	22.2	25.9	13.9	9.6	11.8	47.6	43.0	44.9
120	4	30.7	21.5	25.5	11.1	9.9	10.4	46.5	34.5	41.4
150	1			32.0			14.3			44.6

the majority being between eighteen and twenty-two years. The number of previous pregnancies recorded ranged from 0 to 8 with a considerable proportion of primiparae.

In the interest of space economy we have refrained from tabulating all our results, but in Table I have presented the maximum, minimum

VARIATION OF THE RATIO UREA NITROGEN: NONPROTEIN NITROGEN DURING PREGNANCY

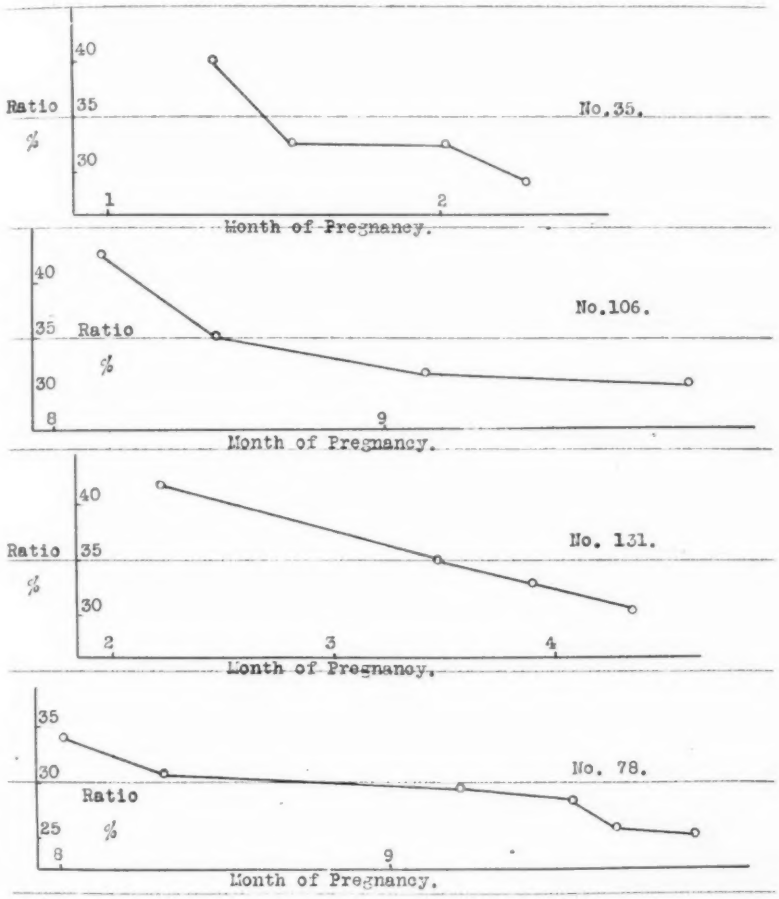

Fig. 1.

and average figures obtained on our antepartum series, while in Table II we give the same data for our postpartum observations.

In 24 cases we were able to obtain several samples of blood at intervals of a month or more during the antepartum period, and in several instances it was also possible to repeat these observations after delivery. Several curves prepared from the data obtained in these latter cases are presented in Figs. 1 and 2.

SUMMARY

Our results may be briefly summarized. In the normal pregnant woman there was observed in the majority of cases a slight decrease in the concentration of nonprotein nitrogen of the blood which is accompanied by a relatively large decrease in the urea nitrogen fraction.

VARIATION OF THE RATIO UREA NITROGEN: NONPROTEIN NITROGEN DURING PREGNANCY

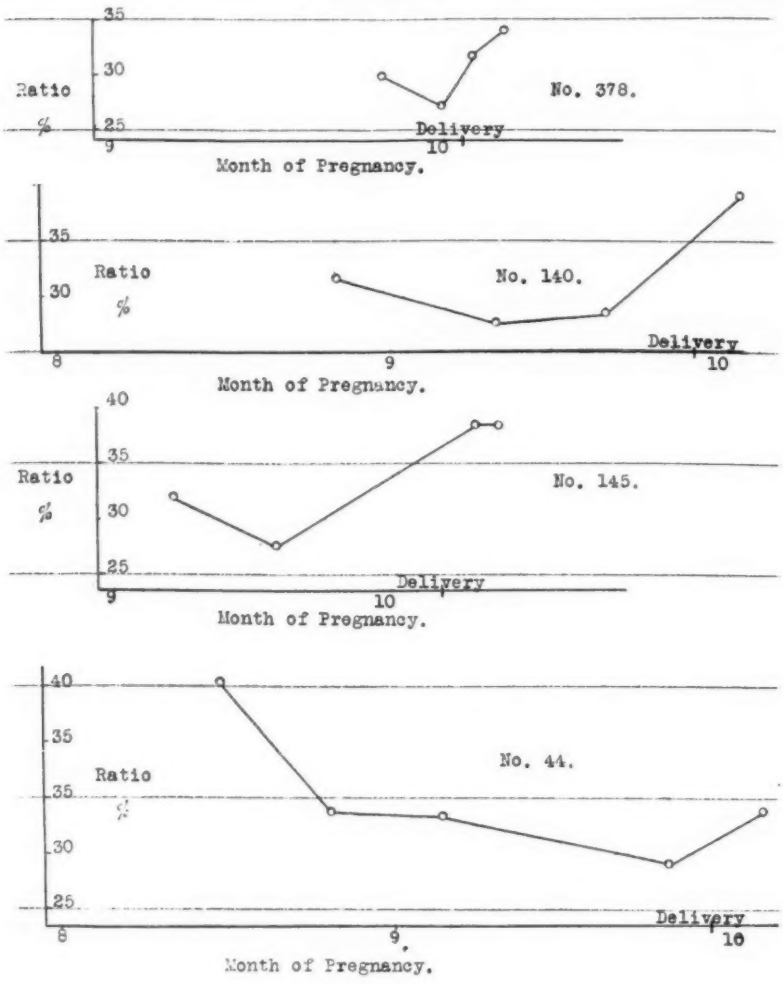

Fig. 2.

Values for urea nitrogen of over 10 mg. per 100 c.c. of blood were noted in less than 4 per cent of our cases, while results as low as 5 mg. of urea nitrogen per 100 c.c. of blood were obtained. Needless to say such abnormal values as the one just cited were checked by repeated analyses, so that we felt reasonably sure that they were not due to analytic errors.

The average figures presented in Table I show a slight but gradual decrease in the ratio of urea nitrogen to nonprotein nitrogen during the course of pregnancy, while the results on postpartum blood given in Table II indicate an equally definite and gradual rise in this ratio.

This fall in the urea nitrogen, nonprotein nitrogen ratio during the advance of pregnancy with the subsequent rise during the postpartum period is also shown graphically in Figs. 1 and 2.

The following figures in the different types of cases studied also offer further evidence for our conclusion that in pregnancy the ratio of urea nitrogen to total nonprotein nitrogen in the blood is lower than in nonpregnant individuals.

Average ratio of urea nitrogen to nonprotein nitrogen in the blood:

In 162 normal pregnant women	33.1
In 55 women eleven hours to five months after delivery	42.6
In 4 normal nonpregnant women	45.6
In 10 normal men	48.5

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A COMPARATIVE STUDY BASED ON FIVE HUNDRED CONSECUTIVE CASES OF INDUCTION OF LABOR*

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A SUCCESSFUL method of inducing labor is a necessary part of the armamentarium of every obstetrician. To be completely successful such a method must not only initiate labor in a large percentage of cases but must also assure mother and fetus the greatest possible degree of safety. Many methods are described in the literature. Of these, some are successful but dangerous to mother or fetus, others carry no increased fetal or maternal morbidity or mortality but are successful in only a small percentage of cases.

The first recorded induction of labor was done in 1738 in England when Mary Donnelly ruptured the membranes in a patient with contracted pelvis in order to induce premature labor. The next recorded method was devised by Kluge who inserted sponge tents into the cervix. Simpson and Scanzoni each attempted the induction of labor by injecting carbonic acid gas into the uterus. Krause, in 1855, reported the method now known by his name, namely, the insertion of soft rubber bougies between uterine wall and fetal membranes. Kiwisch sought to induce labor by alternating hot and cold vaginal douches. All of these methods were unsatisfactory in that labor was induced in only a comparatively small percentage of cases.

The most successful of the above procedures is the Krause method. This has many adherents even today. Among these Bauld[1] reports that 60 to 70 per cent are successful, and Davis[2] recommends bougies as being "highly successful and never dangerous." Hewitt[3] believes the method to be of value but warns especially against the rather large percentage of failure and the increased incidence of local infection and sepsis following its use. That the method also carries a definite risk from trauma as well as from infection is attested to by the reports of Robinson[4] and others who report severe hemorrhages following perforation of the placenta by the bougies. This is prone to occur especially in those patients in whom the placental site is low.

In 1888 the de Ribes bag was devised as a means of initiating labor. This was later modified by Barnes and also Voorhees, and today these three types are still of value. Bag induction, while it has proved very efficient, must of necessity carry an increased morbidity and mortality. Passing the bag through the vagina into the cervix together with the fact that it remains in place for several hours, increases the possibility of uterine contamination by vaginal bacteria.

In an attempt to avoid such an increase in morbidity and mortality, Klein[5] has recently developed a procteurynter, which in his hands was successful in 60 per cent of a series of 800 cases. Nettlesheim[6] found this method successful in only 46 per cent of his patients. Baum[7] has replaced the rubberized bag by a sheep bladder which is inserted through the cervix and is then filled with glycerin. This increases in size while in the uterus by the process of osmosis, and thus stimulates labor pains. Neither Baum nor Sztehlo[8] who also recommend this procedure give their percentage of success or their morbidity figures. Druskin[9] used pigs' bladders filled with glycerin in a series of 84 patients, some of whom also received castor oil and small doses of pituitrin, and reports that 97 per cent were successful.

*Read at a meeting of the Chicago Gynecological Society, May 18, 1928.

The induction of labor by medicinal means has received a great deal of attention because of the fact that there is no increase in maternal infection from vaginal or intrauterine manipulation. Castor oil is well-known for its stimulation of smooth muscle and of the lower sympathetic nerve centers. Its powers are enhanced when combined with an oxytoxic, such as quinine. The administration of castor oil is therefore frequently followed by quinine either in broken and frequent doses or in one to three larger doses. Muschallik[10] reports 58.6 per cent success in his series of inductions by means of castor oil and quinine, Bailey[11] had 72.7 per cent success in 55 patients, and Johnston[12] had 63 successful inductions in 80 patients, an incidence of 79 per cent.

The use of quinine is not entirely free from danger. Williamson[13] who used castor oil and quinine with success in only 46.6 per cent of his series of 300 patients, reports several cases of marked cinchonism. Gellhorn[14] has reported two fetal deaths following the use of quinine. Torland[29] has recently described a similar case.

Since Oliver and Shafer[15] isolated the physiologically active substance of the pituitary gland in 1894, and Blair Bell[16] found that this substance produced and stimulated uterine contractions in rabbits, many investigators have attempted to induce labor with pituitary extracts. Fries[17] and Studeney[18] in 1911 were the first to report successful inductions of labor by hypodermic injections of this substance. Stein and Dover[19] in 1917 reported 34 patients in whom labor was induced by castor oil followed by three minim doses of pituitary extract. They were successful in 60 per cent of these. A. Stein[20] succeeded in inducing 70 per cent of his patients by giving two ounces of castor oil followed by two minim doses of pituitary extract at hourly intervals. Watson[21, 22] followed one ounce of castor oil and three ten-grain doses of quinine by injections of one half cubic centimeter of pituitary extract every thirty minutes. In 75 per cent of his patients, labor began at once. Browne[23] using the Watson technic in 44 patients was successful in 90 per cent but had four stillbirths from this method. One of these he attributes to the use of the pituitary extract. Watson in 195 inductions had a fetal mortality of 6.5 per cent. Scott[24] modified the Watson technic by decreasing the dosage of pituitary extract in order to avoid this excessive fetal mortality and in 198 patients was successful in about 90 per cent. He had no fetal deaths which he could attribute to the use of the pituitary extract. Mathieu[25] reduced the pituitary extract to three minims every thirty minutes following the castor oil and quinine, and in 72.5 per cent was successful in starting labor. Williams[26] found the Watson technic to be 80 per cent efficient and had no untoward results from either the quinine or the pituitary extract. Cron[27] used castor oil and quinine followed by five minim doses of pituitary extract in 45 patients and succeeded in 69 per cent.

While pituitary extract has many adherents, it has also been denounced frequently in the literature because of its supposed inefficiency and more especially because of the increased fetal mortality following its use. Bailey[11] condemns its use, and Polak[28] has recently stated that "the employment of pituitrin to induce labor is hazardous and in view of the fact that we have many excellent safe methods, pituitrin should be kept for the third stage of labor only."

This investigation which includes the results of 500 consecutive inductions of labor in 430 patients was undertaken as a means of comparing the various methods of induction of labor now in use. It was felt that more definite conclusions could be drawn from the results obtained when the different methods were used in one obstetric clinic than by attempting to compare the results of one method as used in one clinic with the results of another technic as used in a different clinic. This series covers the period Jan. 1, 1925, to April 1, 1928, in

the obstetric department of the Michael Reese Hospital and includes all of the inductions of labor during this period in patients who were calculated to be more than thirty-eight weeks pregnant.

Indications.—Of the 430 patients, 253 had normal pregnancies and labor was induced at term. One hundred twenty-two were calculated to be 41 to 44 weeks past the last menstrual period when the induction was done. In 33 patients labor was induced because of toxemia, 16 being between thirty-eight to forty weeks pregnant, in 7 because of contracted pelvis and in 4 because of the death of the fetus. There were also 4 patients with placenta previa, 2 with cardiac disease, 2 with severe pyelitis, 2 with transverse presentations, and 1 with an abruptio placentae.

Indications

At term	253	Placenta previa	4
Past term	122	Cardiac disease	2
Toxemia	33	Pyelitis	2
Disproportion	77	Transverse	2
Dead fetus	4	Abruptio placentae	1

Induction Rate.—In 388 patients the induction of labor was successful. In 26 patients a second induction was done, in 7 there were three attempts, in 6 there were four attempts and three patients were induced five times before labor set in. In this series no attempted induction was considered successful unless labor set in within twelve hours after the induction was begun.

Methods.—Six methods of induction were tried. In the first group, castor oil, two ounces, was used and in the second group the castor oil was followed by quinine, five grains every hour until labor began or until three doses had been given, the fetal heart tones being controlled before each successive dose. In the third group the castor oil was followed by one minim doses of pituitrin. The first dose was injected at the height of the castor oil irritation and was repeated every thirty minutes until labor set in or until a maximum of eight doses had been given, the fetal heart tones being controlled before each successive dose. In the fourth group one minim doses of pituitrin were given without the castor oil, the same technic of administration being employed. In the fifth group castor oil, quinine, and pituitrin were used. First the two ounces of castor oil were given followed by five grains of quinine in one and two hours. One-half hour after the second dose of quinine, one minim doses of pituitrin were started and were employed as in the other groups. In the sixth group induction was done by means of a Barnes' or Voorhees' bag.

In addition there was a large number of patients in each group in whom the membranes were stripped or separated from the lower uterine segment. Vaginal examination upon admission is, with certain exceptions, routine in the Michael Reese Hospital. This has previously

been shown to be harmless,[29] and without effect upon puerperal morbidity. During such a vaginal examination it is a simple matter, if desired, to insert the finger through the cervix and by a sweeping motion, around the inner circumference of the lower uterine segment, to separate the membranes. This maneuver must, of course, be gentle in order to avoid rupturing the membranes and is aided, when necessary, by pressing the head into the pelvis with the abdominal hand. The criterion of a successful stripping is a blood stain on the examining finger. The remaining patients in each group were examined vaginally but separation of the membranes was carefully avoided.

Castor Oil.—There were 119 patients induced by castor oil. Of these, the membranes were stripped in 70 and in the remaining 49 no cervical manipulation was done. In the latter group there were 29 primiparae and 16 (55 per cent) went into active labor. Ten of the 20 multiparae (50 per cent) also responded to the castor oil. Of the 70 patients in whom the membranes were stripped, there were 38 primiparae and 30 (79 per cent) went into labor; there were 32 multiparae and 24 (75 per cent) went into labor. The delivery was spontaneous in 53 (66.2 per cent), low forceps were used in 24 (30 per cent), midforceps in one (1.3 per cent) and cesarean section was done twice (2.5 per cent) for failure of engagement of the fetal head. The gross morbidity for the group was 11.3 per cent. In this report gross morbidity includes every patient with a puerperal complication and every patient whose temperature reached 100.4° F. one or more times. The corrected morbidity includes only those patients in whom a definite complication developed. For this group the corrected morbidity was 6.3 per cent due to five patients with foul lochia without fever. Among the 119 babies there was one baby with asphyxia livida who recovered spontaneously. There was no fetal mortality.

Castor Oil and Quinine.—Ninety-eight patients were given castor oil and quinine to induce labor. In 60 the membranes were stripped and of the 28 primiparae, 24 (86 per cent) went into labor; 25 (78 per cent) of the 32 multiparae responded. Eleven (69 per cent) of the 16 primiparae and 13 (59 per cent) of the 22 multiparae whose membranes were not stripped went into labor. The delivery was spontaneous in 56 (76.7 per cent), low forceps were used in 12 (16.4 per cent), in two breech extractions were done (2.7 per cent) and three (4.2 per cent) were delivered by cesarean section on account of relative disproportion. The gross morbidity was 16.4 per cent and the corrected morbidity was 4.2 per cent due to one patient with sapremia and two with foul lochia.

Castor Oil and Pituitrin.—Castor oil and pituitrin were used to induce labor in 142 patients. In 113 of these, the membranes were stripped and 34 (74 per cent) of the 46 primiparae and 60 (89.5 per cent) of the 67 multiparae responded. In 29 patients no stripping

was done and 4 (56 per cent) of the 7 primiparae and 16 (73 per cent) of the 22 multiparae went into labor. There were 85 (74.6 per cent) spontaneous labors, 20 (17.5 per cent) deliveries by low forceps, 7 (6.1 per cent) deliveries by midforceps, and one (0.9 per cent) delivery by high forceps. One patient was delivered by version and extraction for face presentation (0.9 per cent). The gross morbidity was 15 per cent and the corrected morbidity was 8.7 per cent due to three patients with mild sapremia, five with foul lochia, one with pyelitis, and one with a left thrombophlebitis. The fetal mortality was 1.8 per cent due to two fetal deaths, and the fetal morbidity was 1.8 per cent due to one baby with a fractured claviele and one with cerebral hemorrhage with apparent recovery.

The average number of one minim doses of pituitrin was seven and in the successful group the average number of doses was 3.4. There was one case of mild uterine tetany lasting for twenty minutes. This followed the second one minim dose of pituitrin in a twenty-six-year-old primipara in whom induction was done in the thirty-ninth week of pregnancy on account of a preeclamptic toxemia. No treatment was required for the tetany. The remainder of the labor was uneventful, a live baby being delivered spontaneously six hours after the induction was started.

Pituitrin.—Forty-one patients were given pituitrin. In 19 the membranes were stripped and of the 8 primiparae, 4 (50 per cent) responded and of the 11 multiparae, 1 (9 per cent) responded. In 22 patients the membranes were not stripped. There were 6 primiparae and 3 (50 per cent) went into labor; there were 16 multiparae and in 5 (31 per cent) the induction was successful. There were 10 spontaneous deliveries (84.6 per cent), and 2 low forceps deliveries (15.4 per cent). There was a morbidity of 7.7 per cent due to one patient with a foul lochia. One baby had an asphyxia livida which was overcome by means of a tracheal catheter.

Castor Oil, Quinine and Pituitrin.—Induction of labor was attempted in 62 patients by means of castor oil, quinine, and pituitrin and in 51 of these the membranes were stripped when the oil was given. Fourteen of these 51 were primiparae and 13 (91 per cent) went into labor; 37 were multiparae and 35 (94.6 per cent) responded. In 2 (50 per cent) of the 4 primiparae and in 6 (86 per cent) of the 7 multiparae in whom no stripping was done, labor set in. The delivery was spontaneous in 38 (68 per cent); low forceps were used in 13 (23.2 per cent), midforceps in 3 (5.2 per cent), and high forceps in one (1.8 per cent). One patient was delivered by a cesarean section after a fourteen-hour test of labor in which there was failure of engagement of the fetal head.

Bag Induction.—Labor was induced in 38 patients by means of a bag. Of these ten were primiparae and 28 were multiparae. In 36

(94.7 per cent) the induction was successful. Delivery was spontaneous in 21 (58.3 per cent), by low forceps in 7 (19.4 per cent), by mid forceps in 2 (5.6 per cent), by high forceps in one (2.8 per cent), and by version and extraction in 5 (13.9 per cent). There was one maternal death from the effects of a severe postpartum hemorrhage followed by shock. The patient was a twenty-six-year-old primiparae who was very stout and had a masculine type of pelvis. After eight hours of labor the head was engaged but in spite of strong, frequent pains the cervix did not dilate. A Barnes' bag was inserted to hasten dilatation, and, after four hours, the delivery was effected by midforceps. A postpartum hemorrhage of approximately 500 c.c. resulted and the foot of the bed was elevated on account of the ensuing shock. During the next twelve hours there was a persistent trickling of blood from the uterus and the patient died in spite of blood transfusion, and treatment of the shock. The gross morbidity was 33.3 per cent and the corrected morbidity was 27.8 per cent due to two intrapartum infections, four patients with sapremia, five with foul lochia and one patient who developed a puerperal sepsis and thrombophlebitis, from which the recovery was protracted but complete.

RESULTS

A comparison of the various methods of induction employed shows that pituitrin alone is the least efficient, only 31 per cent of the 41 patients responding. Of the 119 patients in whom castor oil was given, 67 per cent responded. When quinine was added to the castor oil 75 per cent went into labor and when pituitrin was added to the castor oil 80 per cent responded. The best results, 90 per cent, were obtained by a combination of castor oil, quinine, and pituitrin.

The percentage of success in those patients in each group in whom the membranes were stripped is markedly increased over the results obtained in those in whom no stripping was done. Fifty-three per cent responded to the castor oil but when the membranes were stripped at the time that the castor oil was given, the percentage of success increased to 77 per cent. In the castor oil quinine group, stripping increased the satisfactory results from 63 per cent to 81 per cent. In the castor oil pituitrin group only 69 per cent responded but when stripping was added, there was a response in 83 per cent. When pituitrin was used alone 26 per cent went into labor and when the membranes were stripped, 36 per cent went into labor. Following the administration of castor oil, quinine, and pituitrin, 73 per cent responded but when, in addition, the membranes were stripped 94 per cent resulted in active labor. The introduction of a bag produced labor in 95 per cent of the patients.

The average time interval that elapsed between the beginning of the induction and the onset of labor was the same for the group in whom the membranes were stripped and those in whom no stripping was done. The average time for primiparae was three hours and thirty-five minutes and for multiparae was two hours and forty-five minutes. The average length of labor for primiparae was sixteen and one-half hours and for multiparae was seven and one-half hours. It would seem, from these figures, that, while stripping the membranes increases the percentage of patients who respond to induction methods, there is no effect upon either the speed of the response to induction nor upon the length of the resulting labor. The average length of labor for both primiparae and multiparae is approximately the average one for labors in general following spontaneous onset. Induction methods apparently have no effect upon the length of labor.

Parity.—There is a very definite feeling in the literature on induction that multiparae show a greater percentage of response to induction methods than do primiparae. From this investigation it would seem that such is not the case. Of the group in whom inductions were done without stripping 58 per cent of the primiparae and 57.5 per cent of the multiparae responded. Of the group in whom inductions were done with stripping, 78.4 per cent of the primiparae and 80 per cent of the multiparae responded. Apparently primiparae respond to induction methods to the same degree as do multiparae.

Delivery.—The incidence of operative delivery is not effected by the induction of the labor. In this series of inductions, 73.5 per cent delivered spontaneously, 18.8 per cent were delivered by low forceps, 3.1 per cent by midforceps, 1.0 per cent by high forceps, 2.2 per cent by version and extraction and 1.4 per cent by cesarean section. In the years 1926 and 1927, the corresponding figures for all patients delivered in the obstetric departments of the Michael Reese Hospitals are spontaneous delivery 70.1 per cent, low forceps 19.3 per cent, midforceps 6.7 per cent, high forceps 0.9 per cent, version and extraction 0.7 per cent, and cesarean section 2.3 per cent.

Morbidity.—During the year 1926 to 1927 the gross morbidity in the obstetric department was 8.6 per cent and the corrected morbidity was 5.1 per cent. In this series the gross morbidity, exclusive of bag inductions, was 11.3 per cent and the corrected morbidity was 6.3 per cent. In the group in whom no stripping was done, the gross morbidity was 10.5 per cent and the corrected morbidity was 5.8 per cent. In the group in whom the membranes were stripped, the gross morbidity was 11.6 per cent and the corrected morbidity was 6.4 per cent. It would seem from a comparison of these figures that the medicinal induction of labor increases the gross and corrected morbidity by 15 to 20 per cent. The increase, when stripping is added is between 25 and 30

per cent. Both of these increased morbidity rates are, however, considerably less than the rates following induction by bag insertion.

Fetal Mortality and Morbidity.—The gross fetal mortality for all full-term pregnancies and deliveries at Michael Reese Hospital is 3.1 per cent and the gross fetal morbidity is 4.9 per cent. In this induction series the fetal mortality was 0.7 per cent and the fetal morbidity was 2.8 per cent. Induction of labor is apparently not dangerous to the fetus.

Repeated Inductions.—There is a small but definite group which seems to resist induction by practically all methods. In this series, there were six patients in whom four inductions were done and three patients in whom five attempts were made. Of the latter, one was a twenty-one-year-old primipara at term, in whom the membranes were stripped when the castor oil was given. The second attempt was by castor oil and quinine two days later. The last three attempts were at forty-eight-hour intervals and were by castor oil and pituitrin. She delivered spontaneously twenty-four hours after the last attempted induction. The second patient, a thirty-two-year-old para ix, was at term and failed to respond to membrane stripping and castor oil, castor oil and pituitrin, castor oil and quinine twice, and finally castor oil. She was allowed to go home and returned in six days in spontaneous labor. She was delivered of a 4200 gm. baby which was healthy and quite apparently overdue. The third patient was a thirty-year-old para iv, estimated to be forty-two weeks pregnant. She was given castor oil on two successive days, castor oil, quinine, and pituitrin on the fourth day, castor oil and pituitrin on the sixth day, and on the eighth day a Voorhees' bag was inserted. She was delivered spontaneously after a six-hour labor and the recovery was uneventful. The baby was a healthy girl weighing 3874 gm.

SUMMARY

This is a report of 500 consecutive inductions of labor in 430 patients all of whom were past the thirty-eighth week of pregnancy. In 338 patients the induction was successful. In 26 patients there were two inductions and in 16 patients there were three to five inductions. Six methods were tested. Pituitrin alone was successful in 26 per cent, castor oil in 53 per cent, castor oil and quinine in 63 per cent, castor oil and pituitrin in 69 per cent, castor oil with quinine and pituitrin in 73 per cent, and bag insertions in 95 per cent. Stripping the membranes markedly increases the percentage of success in each group. After the membranes were stripped, pituitrin was successful in 36 per cent, castor oil in 77 per cent, castor oil and quinine in 81 per cent, castor oil and pituitrin in 83 per cent, and castor oil with quinine and pituitrin in 94 per cent. Primiparae respond to induction methods to the same degree as do multiparae. Stripping the membranes does not hasten

the onset of labor nor shorten the duration of labor. The medicinal induction of labor raises the gross and corrected morbidity from 8.6 per cent and 5.1 per cent to 10.5 per cent and 5.8 per cent respectively. When stripping is added, the morbidities increase to 11.6 per cent and 6.4 per cent respectively. The morbidity following bag inductions in this series is 33.3 per cent and 27.7 per cent respectively. There is no effect upon fetal mortality or morbidity.

CONCLUSIONS

1. The most efficient method of medicinal induction of labor, at or near term, is castor oil, quinine, and pituitrin.

2. The efficiency of all medicinal methods tested is materially enhanced by the stripping of the membranes.

3. Induction methods, at or near term, are as efficient in primiparae as in multiparae.

4. Induction of labor does not affect the character of the delivery.

5. Morbidity without stripping was slightly greater than the morbidity in the obstetric department as a whole; the addition of stripping resulted in a further increase in morbidity. However, these figures are still approximately only one-third of those following bag induction in this series.

6. Induction of labor is apparently not dangerous to the fetus.

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(For discussion, see page 419.)

HEMIPLEGIA DURING PREGNANCY, WITH THE REPORT OF A CASE*

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(From the Obstetrical Service, Evanston Hospital)

ONLY a few cases of hemiplegia with onset during pregnancy have been reported and practically all of these seem to have resulted from cerebral thromboses. Lafon's admirable review of the literature in 1896 revealed 25 cases; in 1925 Talley and Ashton were able to add only 17 more. A recent search of the literature failed to find any additional cases. The case here reported is the only one that occurred during the pregnancies of the last 5,000 women delivered at the Evanston Hospital.

The hemiplegias due to cerebral thrombosis nearly all occur in the first three weeks of pregnancy. The cause has been traced to some focus of infection in about 75 per cent of instances. In all cases reported there were no deaths and about 50 per cent made a partial or complete recovery.

The case reported here occurred in Mrs. N., 25 years old, para ii, who presented herself for prenatal care March 15, 1926, in the second month of her pregnancy. The general examination was negative. There were no complaints. The blood pressure was 112/82 and the urine was negative. From March 15 to September 6 the patient was seen at the office every second week. The systolic blood pressure varied between 98 mm. and 112 mm. of mercury. There seemed to be nothing unusual about the patient's progress until during an office call late in July she mumbled something unintelligible and began to cry. She explained with difficulty that it was hard for her to form the words that expressed her thoughts. As the patient was of a rather excitable temperament, the condition was attributed to an attack of hysteria and triple bromides were prescribed. That evening she reported herself much improved. From this time until September 13 attacks similar to the one just mentioned occurred on several occasions, usually when the patient was very tired or had had some undue excitement. Each attack subsided following administration of bromides. On the evening of September 13, 1926, after spending an unusually quiet and pleasant day at her mother's home and feeling exceptionally well, the patient was preparing to retire when she was seized with a feeling of tiredness and a sensation of numbness on the right side of the face and in the right arm and leg. Immediately afterward she discovered that she could not move her right arm or leg. Upon endeavoring to call her husband from an adjoining room, she found that she was unable to talk plainly. The author saw the patient within an hour following the attack. A rather superficial examination revealed a paralysis of the right side of the face and of the right arm and leg. The patient was very much upset, alternately crying and laughing. Still being of the opinion that the symptoms were probably due to hysteria an effort was made to quiet the

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patient with sedatives but with no avail. The following morning Dr. L. J. Pollock was called in consultation. He wrote concerning his findings and opinions in a letter as follows:

"When I examined Mrs. N. on September 15, 1926, I found a right-sided hemiplegia, with rather marked rigidity and involuntary movements of the right arm. The deep reflexes of the right side were markedly increased, and an ankle and knee clonus was elicited. There were Babinski, Oppenheim and Chaddock reflexes on the right side, and the abdominal reflexes were diminished on both sides. The visual fields grossly were normal and ophthalmoscopic examination failed to reveal any pathology. Although prior to my examination there had been very slight diminution of sensation on the right, when I examined her there was considerable loss of deep sensibility particularly in the right arm. A rather severe grade of transcortical aphasia was present. Considering the history of recurrent attacks of what might be interpreted as focal or cortical fits or of slight attacks such as one would get from a vascular spasm, it was necessary to exclude a possible cerebral neoplasm. The subsequent course with absence of any evidence of increased intracranial tension, headache, vomiting, or choked disc, slow pulse, etc., suffices to exclude a neoplasm. The negative serologic picture was sufficient to exclude the possibility of syphilis of the nervous system. One is, therefore, compelled to conclude that we are dealing with some type of vascular pathology, which may be either a thrombosis or an embolism. I was unable to determine any possible predisposing illness which would produce a thrombus. Emboli, although frequent after childbirth, occur during pregnancy as well. The numerous attacks speak more for thrombus than for embolus. They both result in a pneumonic infarct, giving about the same prognosis. I would expect a gradual improvement in motion and a diminution in spasticity and involuntary movements in the arm as well as complete recovery of the leg and speech."

The patient was sent to the Evanston Hospital. X-ray examinations of the head revealed no evidence of brain tumor or increased intracranial pressure. Spinal puncture revealed a negative spinal fluid, Wassermann tests on spinal fluid and blood were negative. Blood counts and urine were negative, and temperature was normal.

The treatment consisted entirely of complete rest in bed. Speech improved and there was a slight return of movement in the arm and leg. On Octobr 14 labor was induced by routine methods, and a normal eight hour multiparous labor and spontaneous delivery with a normal living child resulted. After two weeks, passive motion and gentle massage were instituted. The patient left the hospital on December 8, 1926, eleven weeks after her hemiplegic attack and seven weeks after delivery. She was able to walk and to use her arm and leg fairly well. Improvement was most evident in her speech, which was practically normal. Physiotherapy treatment was continued for one month when the patient left the city. Following an examination March 2, 1928, Dr. Pollock wrote,

"I re-examined Mrs. N. on March 2. She shows very remarkable improvement. At the present time she shows a right hemiparesis which is observed in her gait and which is characterized by slight rigidity of the right leg and in slowness and some clumsiness of movements of this leg and in slight incoordination and weakness of the right upper extremity. A considerable degree of intentional hypertonia is seen in the upper extremity, wherein after flexing the fingers the intended extension is interfered with by a persisting flexor contracture. The deep reflexes of the right side are increased as compared to the left. A right ankle clonus and knee clonus are found. The superficial abdominal reflexes are diminished on the right side, and a Babinski is present. There was no objective loss of sensation and no astereognosis.

The paraplegia had practically disappeared but occasionally some hesitation in the selection of words was noted. Ophthalmic examination of the visual fields showed normal findings.''

SUMMARY

A report of a case of hemiplegia during pregnancy and a reference to the literature revealing 42 previously reported cases is made. It is reassuring to the obstetrician to know that this condition in no way complicated labor in any instance and that a large percentage of the patients recovered completely from the hemiplegia.

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(For discussion, see page 419.)

CESAREAN SECTION

A Review of 109 Cases*

By Clifford B. Lull, M.D., Philadelphia, Pa.

(From the Philadelphia Lying-In Hospital)

THERE have been delivered at the Lying-In Hospital from October 1, 1924, to October 1, 1927, 2161 women. Among these, delivery by abdominal hysterotomy has been thought necessary one hundred and nine times. A review of these case histories forms the basis of this paper.

Statistics, as a rule, are uninteresting to most of us but it is the only way that we can accurately check our work, and allow us to compare our results with that of other clinics. It is a well-known fact that statistics can be made to fit the occasion, and although it hurts at times, it does us all good to know that none of us are perfect.

I will not attempt in this paper to compare these figures with other statistics in the literature but I am placing them before you to judge for yourselves.

It might be well to state that there are two services at the Lying-In Hospital which run concurrently through the entire year. These two

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services alternate cases on admission so that at the end of the year a like number of cases have been treated by each service. As there is no courtesy staff, all of these patients have been operated upon by one of the members of the staff and are about equally divided between the two services. As a general rule, at least two members of the staff have seen all the cases requiring cesarean section, before operation.

One hundred and nine (109) cesarean sections in 2161 deliveries give an incidence of 5.4 per cent.

The youngest patient operated upon was fourteen years of age, the oldest forty-three years, with an average of twenty-two years.

The colored race is more prone to have pelvic deformities than the white. There were 52 white women and 57 colored. As there were more colored than white in the total number of deliveries, the incidence of section was higher among the white women.

Seventy-seven of these patients were primiparae. One was a para viii who had a ruptured uterus on admission, one para v who had acute polyhydramnios with twin pregnancy at four and a half months, complicated by cardiorenal disease. One was a para iv who had had three previous sections. The remaining 29 patients were para ii who had had previous sections, mostly for contracted pelvis.

The indications for operation were as follows:

(a) Absolute contraction of the pelvis, 14 of whom had had previous sections	30
(b) Borderline contractions, all of whom were given a test of labor	43
(c) Contracted pelves of various degrees and previous cesarean sections	11
(d) Fibroids of the uterus interfering with descent of the head	2
(e) Premature separation of normally implanted placenta	2
(f) Central placenta previa	5
(g) Failure of dilatation of the cervix	4
(h) Epilepsy and sterilization	1
(i) Varicosities of the vulva and vagina	1
(j) Ruptured uterus	1
(k) Preeclamptic toxemia	3
(l) Acute polyhydramnios, cardiorenal	1
(m) Cardiac disease	2
(n) Hernia of the uterus	1
(o) Separation of the symphysis and tuberculosis of the hip	1
(p) Dystocia due to previous operation on the uterus	1

It is our general rule to operate upon patients who have an internal conjugate of less than 8 cm. at the time of election and classify them as absolute contractions. The borderline case is allowed to go into labor and if, after a test of labor, averaging about eight hours, there is no attempt at engagement, section is done. This is the type of case which offers more opportunity for poor judgment than any other type of obstetric patient. All of our patients who had had previous cesarean sections were again sectioned.

Fibroids are considered an indication when they obstruct the birth canal. Premature separation of a normally situated placenta with no dilatation of the cervix and marked internal hemorrhage was the indication in two cases. All of our patients with central placenta previa were sectioned.

That the cervix of some primiparae around forty years of age does not dilate, was borne out in four cases. These patients all had a definite test of labor, at the end of which time they evidenced no progress in effacement or dilatation. Living babies were obtained in each case and all made uneventful recoveries.

The one case of epilepsy was mentally deficient, her morals were unspeakable and she was sectioned and sterilized at the request of her family. The one case of varicosity was in such condition that it was impossible to even make a vaginal examination.

In these two thousand cases, we had one ruptured uterus, an emergency case who had been in labor twenty-two hours before admission in a moribund condition.

The only indication for abdominal section in eclampsia we believe to be in an elderly primipara who, after several hours of eliminative treatment, shows no ability to dilate her cervix or improve in general condition. In preeclamptic toxemia, occurring in the latter months of pregnancy, especially in a primipara where treatment over a period of several days shows no improvement, the uterus can be emptied with safety by the abdominal route. The risk can be definitely diminished by use of local anesthesia.

There are certain types of cardiac disease complicating pregnancy upon whom the strain of labor might end in cardiac dilatation. Although the risk is great either way, section, especially under local anesthesia, certainly saves some of these women. How much a heart can stand is rather a difficult question to settle, as was brought out by one of these cardiac cases. The consultant cardiologist estimated in this patient that she would die no matter how she had her baby. This patient made an uneventful recovery after section with local anesthesia. Her physician reports her in good condition one year later.

The hernia of the uterus was accompanied by left torsion and transverse position. The one case of dystocia, caused by previous operation on the uterus, had had two previous abdominal operations, was forty-three years of age, and her youngest child was nineteen years old.

Ether was given 104 times, straight nitrous-oxide twice and local anesthesia three times. The question of what anesthesia to use is, I believe, an important one. Ether, if given properly, is unquestionably the safest. Although in this series only three cases were done under local anesthesia, I believe there is a definite field for its use in doing this operation on certain types of individuals.

The classical type of operation was done in all of this series, myomectomy once, celiohysterectomy three times and fifteen patients were sterilized upon whom previous sections had been done.

Our attitude has been to advise sterilization at the time of the second section if both children are alive and the patient desires it. One of these patients upon whom we did the fourth section was supposed to have been sterilized at the time of her third cesarean. At operation, it was found that the previous operator, in another city, had resected the fallopian tube on one side but had inadvertently used the round ligament instead of the tube on the opposite side.

Fifty-one of these patients were operated upon before, at the onset, or very shortly after the onset of labor. One patient was in labor sixty-one hours, one forty-eight hours, and one forty-one hours. The average for the other patients was approximately twelve and one-half hours. The patient in labor sixty-one hours had unruptured membranes and had had only one vaginal examination. Where there is definite indication for operation before the onset of labor, no vaginal examinations are made. If the patient is to be given a test of labor, usually one careful vaginal examination is made at the end of the test labor.

One patient in this series had four vaginal examinations before operation. Her membranes were unruptured, however, and she made an uneventful recovery.

One hundred and three patients had unruptured membranes at the time of operation. Six had ruptured but had not been manipulated before admisison to the hospital.

Excluding the mortality, which I shall discuss later, the morbidity had been figured on the same basis as we estimate our normal cases, namely, an elevation of temperature to 100° twice in any twenty-four hours, not including the first twenty-four hours after delivery. The temperature is taken every four hours. Ten patients had no morbidity. The morbidity in the other cases was what we considered normal postoperative reactions, except in the following, which had the associated complications. There occurred:

Thrombophlebitis	4 cases	Engorged breasts	3 cases
Infected wound	3 cases	Influenza	1 case
Pyelitis	2 cases	Tonsillitis	1 case
Bronchopneumonia	3 cases	Sapremia	2 cases
Bronchitis	2 cases	Heat stroke	1 case
Breast abscess	2 cases	Cystitis	1 case

There occurred in this series 7 deaths, a mortality of 6.4 per cent. They were as follows:

CASE 9.—A primipara, twenty-four years of age. The indication for operation was contracted pelvis. She had been in labor on the outside for twenty-two hours. The child was dead in the peritoneal cavity. Hysterectomy was done and the patient died a short time after operation from shock.

CASE 48.—A primipara, eighteen years of age, with contracted pelvis. She died twenty-four hours after operation, from collapse of the left lung. The child is living and in good condition.

CASE 55.—A primipara, seventeen years old, with contracted pelvis. Ether anesthesia, unruptured membranes. Had been in labor fourteen hours. There was a question as to the number of vaginal examinations that had been performed. She died on the fifth day of paralytic ileus. The child is living and in good condition.

CASE 56.—A primipara, twenty-one years of age with contracted pelvis. Had been eight hours in labor and had had one vaginal examination. Had unruptured membranes. Died on the fifth day from large tubo-ovarian abscess. The child is living and in good condition.

CASE 88.—Para ii. First child was stillborn by version; had a contracted pelvis. She was operated on before the onset of labor, had no examinations, membranes were unruptured. Died on the fourth day from peritonitis.

CASE 92.—A primipara, aged thirty-six years, eight months pregnant. Had cardiorenal disease. Operated under local anesthesia and died on the fifth day from complete suppression of urine. She did not respond to medical treatment and it was thought best to terminate the pregnancy.

CASE 106.—A primipara, aged eighteen years, admitted for toxemia also cardiac condition. She was not in labor. Developed a complete premature separation of the placenta while in the hospital ward. Although but a short time elapsed before operation, the baby was stillborn and the mother died of hemorrhage.

One hundred and one patients were discharged in good condition, and although a few were not followed up, the ones who were, have remained in good physical condition.

Nine babies were stillborn or died shortly after birth. Both children of the cases of premature separation were stillborn. One child whose mother had central placenta previa died of prematurity. One child died of an undeveloped pulmonary system and one died of subperiosteal hemorrhage. Also, one died of enlarged thymus and one was definitely luetic. The patient operated upon for epilepsy had a twin pregnancy, both of which died shortly after delivery. All other children left the hospital in good condition. The ruptured uterus case was stillborn.

From a study of these case histories, I would conclude:

1. That we were fortunate in not having more patients referred after ineffectual attempts were made to deliver on the outside.

2. That the case operated upon before, or at the onset of labor had a much less stormy convalescence than a patient operated upon after having been in labor for several hours.

3. That borderline or elective section offers more chance for unwise decision than any of the problems presented to the obstetrician. That the decision to operate in these cases should be made early before the membranes have ruptured and the patient has had numerous examinations.

4. That even the ideal case for section, namely, the patient who has had a definite indication before the onset of labor, who is a good operative risk, whose membranes are unruptured and who has had no vaginal examination, sometimes adds a mortality to our statistics.

1731 PINE STREET.

(For discussion, see page 417.)

PROPHYLACTIC TREATMENT OF PUERPERAL INFECTION BY INTRAUTERINE APPLICATIONS OF ANTISEPTIC SOLUTIONS

BY SAMUEL S. ROSENFELD, M.D., F.A.C.S., NEW YORK, N. Y.

THERE are at present in vogue several methods of performing cesarean section which are more or less efficient in the prevention of general peritonitis. No method, however, can lay claim to the ability of preventing sepsis or puerperal endometritis.

Bacteriologic and pharmacologic studies reveal the causes for the almost universal failure of local treatment once bacteria have gained entrance into the cells. Treatment, to be effective, must be begun before the germs have gotten a foothold. It is much more logical to attempt to prevent sepsis rather than to try to cure it.

The World War has greatly enriched our knowledge of antiseptics, and the best methods of applying them. In the prophylactic treatment of uterine infection one should seek an antiseptic of high germicidal power, simple to prepare, preferably nonirritating to tissues and easy of application. With these criteria in mind neutral acriflavine was chosen. Its antiseptic coefficient is high, and it is nonirritating even in the peritoneal cavity. I injected guinea pigs intraperitoneally with acriflavine solution (1-1000) without any signs or symptoms of peritonitis resulting. Browning and Cohen claim that flavines are of particular value in the prophylaxis of infection, that is, to prevent the occurrence of inflammation and suppuration when applied shortly after the organisms have gained access to the tissues. The activity of flavines is not reduced by protein solutions such as serum.

Browning, Gulbraisen, and Thornton state that flavine compounds may be applied to the peritoneum with safety. In their conclusions they strongly emphasize the value of the flavine compounds, especially for the purpose of preventing the onset of septic manifestations in early wounds. Flavine retains its antiseptic powers when in contact with tissues and infected material for a much longer time than does Dakin's solution, and therefore need not be applied as often as the latter.

A great obstacle encountered by those using intrauterine antiseptics has been the difficulty of keeping the tubes carrying the solutions in

place for any length of time. Uterine contractions force the tubes out within a few hours or a few days. Several more or less ingenious and complicated appliances have been devised to keep the tubes in place. The author, because of its efficacy and its ease of procurement, has found an ordinary rubber T-tube best suited for this purpose. The rubber must be of first quality as it is absolutely essential that the tubes remain patent. The tubes may be obtained ready for use from the dealer, or may be easily fashioned by perforating the upper end of a rubber tube, inserting a cross-piece of rubber tubing and attaching the latter securely by sewing it with silk or linen thread to the vertical tube. Since blood clots and débris can easily block the tubes, these should be perforated in several places so as to insure egress for the antiseptic solution. In the vertical end of the tube the perforations should be made high, just below and above the T cross-piece so as to permit the fluid to exit at or near the fundus. Gravity will then insure that the lower portions of the uterus come in contact with the solution. To insure a return flow and guard against the antiseptic entering the peritoneal cavity through the fallopian tubes, at least two rubber treatment tubes should be introduced into the uterus. In guinea pig experiments I have not been able to produce peritonitis after the injection of human lochia containing saprophytic organisms. Mixtures of lochia and acriflavine also failed to produce peritonitis. I at first tried to use continuous irrigations of warm acriflavine solution (1-1000) but found it impracticable. I now have two tubes irrigated with 30 c.c. each of (1-1000) neutral acriflavine solution every eight hours night and day. In presumably infected cases where cesarean section is indicated and performed, the tubes are introduced through the uterine incision and the lower ends brought out through the vagina, strapped to one thigh and enclosed in a sterile towel. In cases when delivery is effected *per vias naturales*, the tubes are introduced through the cervix with a dressing forceps and affixed to the thigh as described above.

This treatment is indicated in all cases where infection is presumably present. The first three cases in which I employed this method will exemplify the cases suitable for this treatment.

CASE 1.—Mrs. J. W., age twenty-eight, para i. Admitted to Lebanon Hospital Feb. 18, 1928, discharged March 5, 1928. Membranes had ruptured three days before she was admitted into the hospital, "strong pains" commenced twenty-four hours before admission. She was examined many times at home, the attending physician not using gloves. Examination at the hospital revealed that the patient had a generally contracted pelvis, and that the head was unengaged. The author thereupon performed a cesarean section with drainage under local anesthesia, as described by him in the August, 1926 number of the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY. Two T-tubes were inserted through the uterine incision, brought out through the vagina and attached to the thigh. Acriflavine solution (1-1000) was introduced through the tubes every four hours. Three days after operation, a culture from the vagina revealed the presence of the follow-

ing organisims: B. coli, pneumococci, Staphylococcus pyogenes aureus and gram positive, saprophytic bacilli. On the second day after operation the temperature was 103.4°, on the fifth day the patient had a chill and the temperature rose to 105.2°. A leucocyte count on the same day showed W.B.C. 13,600, polys 94 per cent. The temperature came down on the same day and remained normal until discharge from the hospital. The tubes were removed the sixth day after operation.

CASE 2.—Mrs. A. W., aged twenty-five. Admitted to Lebanon Hospital April 15, 1928, discharged May 2, 1928. Membranes ruptured a few hours before onset of labor. The patient had a flat pelvis, and it was deemed advisable to give her a test of labor. After forty-six hours of labor there was no engagement of the fetal head. I thereupon performed a cesarean section employing the same technic as in Case 1. Temperature at time of operation was 101°. The temperature range during her convalescence was between 98.6° and 101.6°. The tubes were removed eight days after operation.

CASE 3.—Mrs. Y. S., aged thirty-eight. Admitted to Lebanon Hospital April 8, 1928, discharged April 19, 1928. On day of admission the patient felt a fetal part protruding from her vagina. This proved to be a hand. The cervix was rigid and tightly enclosed both the arm and forearm. She delivered spontaneously twenty-eight hours after admission to the hospital. Two T-tubes were inserted through the cervix immediately following delivery, and removed April 14, 1928. Patient had no rise of temperature during her entire stay in the hospital.

I do not claim that these patients would not have recovered had they been treated with other antiseptics or even without any antiseptics at all. Dakin's solution, mercurochrome or one of the dyes might be as good or even better. Neutral acriflavine was chosen because on theoretic grounds it seemed to me to be the most suitable antiseptic for this particular work. It is hoped that others employing this procedure will report their results, so that it will be possible to properly evaluate both the efficacy of the antiseptics used and the method in general.

SUMMARY

1. Most good can be obtained from the use of antiseptics if they are applied before the pathogenic organisms have penetrated into the cellular structures.

2. Acriflavine is a suitable antiseptic for intrauterine application.

3. Rubber T-tubes are practicable for intrauterine flushing.

4. Three patients who were presumably infected were treated successfully with intrauterine injections of acriflavine.

In conclusion I wish to express my gratitude to D. A. J. Rongy for his helpful suggestions and kind cooperation.

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2021 GRAND CONCOURSE.

SOME FACTORS IN POSTPARTUM MATERNAL MORBIDITY*

By Owen J. Toland, M.D., Cynwyd, Pa.

THE following study has been made from the records of the Lying-In Hospital of Philadelphia.

The cases are not selected in any way except to exclude the cesarean section cases, as it seems that the procedure is in itself sufficient to produce a morbidity without any extraneous factor.

The criterion of morbidity in these cases is an elevation of temperature to 100° or over twice in any twenty-four hours, not necessarily consecutively, excluding twenty-four hours following delivery; temperatures being taken routinely fourth hour day and night in all patients.

This series consists of 500 cases and includes every type of delivery except cesarean section. In this series there were 128 patients morbid from all causes, a total of 25.6 per cent. In these 128 patients the most frequent factor present was the condition roughly described as blocked lochia. Of these there were 39. In each of these cases there is a note stating that scant lochia corresponding to the elevation in temperature caused the morbidity. This group represents 30.4 per cent of the total morbidity.

The next most frequent cause can be attributed to engorged breasts. There were 34 of these cases which represents 26.5 per cent of the total morbidity.

The third most frequent cause in this series is intercurrent infection, morbidity occurring in 21 cases, or 16.3 per cent. These intercurrent infections include: pyelitis, 1 case; pharyngitis, 2 cases; tonsillitis, 2 cases; bronchopneumonia, 5 cases; Vincent's angina, 1 case; acute arthritis, 2 cases; grippe, 1 case; salpingitis, 4 cases; nephritis, 1 case; fistula in ano, 1.

Fourth in the list came constipation and "no cause discovered," each with 11 victims to their credit. Combined these make up 17.1 per cent.

These five causes aggregate 90.3 per cent of the morbidities. The remaining 9.7 per cent include fissured nipples, 2 cases; cause set down to artificial termination of labor, 2; infected perineal repairs, 7; and hemorrhage, 1.

These statistics are taking a group of 500 cases as a unit.

To see if luetic taint had any influence on the percentage of morbidity, the cases were divided into two groups: luetic and nonluetic in the percentages noted. It is interesting to record that in this series of 500

*Read at a meeting of the Philadelphia Obstetrical Society, November 3, 1927.

cases, coming as they did from the worst elements of the city, there were only 52 with luetic taint. These occurred as followes: 34 cases in which both maternal and cord Wassermanns were positive; 11 cases in which maternal was positive and cord negative; 3 cases in which maternal was positive and cord anticomplementary; 1 case maternal anticomplementary and baby's positive; 3 cases in which maternal was negative and baby's positive.

In the group with a luetic taint, 52 in all, there were 16 morbidities, which gives 30.7 per cent morbid as opposed to 25.2 per cent morbid in the nonluetic group. This figure though somewhat higher is not striking.

When the series was grouped into cases of spontaneous delivery as opposed to those with artificial termination of labor, the result was slightly more clear cut. The total series was 46 cases with artificial termination. Of these 16 were morbid, which gives the figure a 34.8 per cent morbidity as opposed to 25 in the nonoperative group. It is noteworthy that of the 16 morbid cases only 2 were set down as having the morbidity due to the operative procedure.

An attempt was made to establish some relationship between the length of the second stage of labor and the percentage of morbidity, but the figures on the charts were so varied that no logical deduction could be arrived at.

The conclusions to be drawn from this study seem to be:

1. The incidence of maternal morbidity, excluding cesarean section, is about 25.6 per cent, when our standard of morbidity is employed.

2. That luetic taint and operative deliveries have but little influence on the percentage of morbidity.

3. That both maternal and cord Wassermanns should be taken routinely, or many cases with luetic taint will go undiagnosed.

315 Clwyd Road.

(For discussion, see page 416.)

Society Transactions

THE NEW YORK OBSTETRICAL SOCIETY

MEETING OF OCTOBER 9, 1928

DR. T. C. PEIGHTAL presented a case report entitled **Torsion of the Fibromatous Uterus.** (For original article see page 363.)

DISCUSSION

DR. HOWARD C. TAYLOR said that in the case of a large tumor such as this, the diagnosis between a twisted uterus with a fibroid tumor and an ovarian cyst with a twisted pedicle is practically impossible, but it makes no difference so far as the treatment itself is concerned because either condition requires an operation without delay. In a smaller tumor where you can feel definitely a fibroid tumor in the uterus, it is possible to make a diagnosis, but even here most of the diagnoses are made at the time of operation.

DR. E. W. HOLLADAY referred to one point in the differential diagnosis which Dr. Peightal did not bring out and which came up in a case operated on by the late Dr. Studdiford in Bellevue Hospital, which was evidently of the intermediate chronic type and had no acute exacerbation so as to give a clear-cut diagnosis. Degeneration of a fibroid was considered and the condition was found to be a bipolar fibroid accompanying a very early pregnancy in a woman at the menopause. Pregnancy was not suspected and was not noted until after the hysterectomy.

DR. G. L. MOENCH said that these cases are very rare, that Schultze found only 52 reported cases, and saw only 4 of these in 1,000 laparotomies. Dr. Moench has seen 2 cases, one in which the uterus itself and its long, narrow cervix was twisted more than completely around its axis. The other was a case in which a pedunculated fibromyoma was twisted on its axis. Both of these cases are reported in the literature early in 1916.

DR. SYDNEY S. SCHOCHET read a paper (by invitation) entitled **Experimental Endometriosis.** (For original article see page 328.)

DISCUSSION

DR. JAMES EWING spoke of the extreme caution with which the speaker of the evening succeeded in surrounding his work, and, therefore, he felt that almost anything he might say might be open to error. However, it is perfectly obvious that Dr. Schochet has been proceeding upon a very carefully planned system of experiments. If his work had no other value, it would reveal the extreme care which one must observe in undertaking any experiments upon growth in which factors are added, the effects of which he proposes to determine. So many intercurrent factors may come up that the extreme caution which Dr. Schochet has shown is certainly most essential. It is also obvious that any work of this sort must involve a considerable knowledge, not only of normal growth and general physiologic and pathologic conditions but also of chemistry and physical chemistry. Dr. Schochet seemed to him to be one of the first to attempt in a systematic way the control of these physicochemical factors.

While there is in the literature of cancer research today a considerable list of contributions claiming to demonstrate the effects of changes in osmotic tension on the permeability of the cell membrane, on the alkalescence of cell fluids, Dr. Ewing was not convinced that experimenters were sufficiently critical or accurate to warrant any trust in their conclusions. Two authors especially, Watterman and Rodman appeared in London recently at the Cancer Congress with contributions in this field. Their contributions seemed extremely ambitious in the field of speculation and very fragmentary and unsatisfactory in regard to the facts presented. In other words, they had not succeeded in controlling their experiments sufficiently to warrant any conclusions whatever. Dr. Ewing felt that to date there are in the literature no definite proofs that these changes in osmotic tension, or permeability of cell membrane, have actually any effect on the proliferation of tissue cells. If that is the case, then Dr. Schochet has been the first to succeed and is to be congratulated.

Now, the question is: Has Dr. Schochet succeeded in showing that the two sensitizing agents, strontium chloride and iron compounds have been the cause of these rather definite changes in the implanted endometrium? Dr. Ewing's examination of the experimental sections impressed him as having a distinctly different character from the controls, and the sections shown are rather more striking in that respect. Dr. Ewing felt he would like to see a control specimen carried along with each one of these experiments to determine not only whether the cell changes are uniform but also if their tenacity of life is prolonged. If he can show that the sensitized specimens not only show this peculiar proliferation but also that the proliferation goes further and the cells live longer, say, three or four times as long, then the evidence he has would be much more convincing.

Dr. Ewing believed that Dr. Schochet was justified in assuming that the result is due to factors which he introduced. Its bearing upon the question of endometriosis may not be direct. Strontium chloride is not thought of as accompanying the floating fragments of endometrium during menstruation, nor is any other drug, but there may be other chemical agents which do accompany these floating particles.

Dr. Schochet said that hemolytic agents tend to increase the permeability of the cell membrane and to increase oxidation. Hemolytic agents are present in the hemorrhagic fluid of the menstrual flow, and it is not impossible that he will be able to trace in the endometrial fluids chemical agents which may have the same efficacy as strontium chloride and iron.

On the whole Dr. Ewing believed that this study strengthens the belief that loose fragments of endometrium may become implanted, as Sampson and Jacobson have shown, and grow to a larger extent than has been supposed. In other words he substantiates Sampson's theory.

DR. VICTOR C. JACOBSON said that this ingenious method of studying endometrium, by growing it in the anterior chamber of the eye, so that it can be seen from day to day, opens up a considerable field for experimental work and that Dr. Schochet in continuing his study will determine the effect of the various hormones we have at present and combinations of them.

In so far as transplantation of endometrium to the eye is concerned, since it is so far removed from its original source, there is no possibility of local reaction from substances emitted by the uterus through the tube. This method of endometrial culture in the eye offers interesting possibilities in the study of the reactions of this very remarkable tissue. There is, perhaps, no counterpart in human pathology except the ectopic endometrium which we can see at the so-called bleeding umbilicus or in a laparotomy wound. In such locations, after the endometrium has reached a certain size, it is recognized by the patient as being very painful at the time of the menstrual period and is often visible as a bluish or reddish-blue mass which

each month becomes enlarged. Of course, there is considerable tissue overlying such a tumor, skin, subcutaneous and fascial connective tissue, so that in all probability it is not possible to see the more delicate changes take place such as can be followed so well in the experiments by Dr. Schochet in the anterior chamber of the eye.

Dr. Schochet also stated that he has found that the endometrium seemed to have an increased virulence or viability during estrus. At any rate it is apparently more easily transplanted during estrus than when taken during the resting period.

Dr. Jacobson hoped that it would be possible to work out a technic so refined that Dr. Schochet can transplant only epithelium and not stroma cells, or transplant stroma cells and not epithelium. That, he believed, would show the effects of various inorganic and organic substances upon the two main types of cells found in the endometrium. There is much of interest in this for the obstetrician particularly in regard to the question of ectopic decidua. Dr. Jacobson believed that in every full-term pregnancy, careful examination of the tissues of the pelvis will reveal ectopic foci of decidua without any endometrial glands beneath the serosa of the ovary, the posterior wall of the uterus and in the perisinuous tissue of some of the pelvic lymph nodes. It is surprising the wide distribution it has. It is a question whether these decidual cells arise from transplanted endometrial stroma or from fibroblasts which were there all the time but which came in contact with that substance which permits fibroblasts to develop into decidual cells. Dr. Jacobson favored the idea that they are not as a rule due to transplanted stroma cells, unless glands are also present.

DR. ROBERT T. FRANK said that Dr. Schochet in a few words summarized an extensive and controversial literature. Sampson's work has focused new attention upon the origin of endometrium- or adenomyoma-like tissue in the pelvis. Cullen has shown continuous invasion by endometrial glands. Sampson believes in discontinuous metastatic implantation. Others ascribe the seminoplastic deposits to inflammatory metaplasia.

Dr. Schochet found that only uterine musculature implanted in the guinea pig's eye showed rhythmic pulsation, but unfortunately no effort was made to see the difference in implants in the castrated and noncastrated male and female animal. Therefore the full importance of this most interesting observation (rhythmic contraction) cannot be drawn.

The rate of growth of uterine transplants as demonstrated by Frank (published in the Journal of Cancer Research in 1916) is so dependent upon the presence or absence of the female sex hormone, that no conclusions upon the fundamental and tremendously important question which Dr. Schochet raises should be drawn unless this source of error is entirely eliminated. Dr. Frank stressed this particularly because Dr. Schochet had taken such extreme precautions in other directions in order to avoid error both in interpretation and experimentation, and he desired to save him the possibility of being misled by these factors.

Dr. I. C. RUBIN asked if the mitosis was in some respects atypical or always typical. He felt that these cells under abnormal conditions merge or escape from their limiting membrane and present a picture in the syncytial masses that is almost analogous to that seen in so-called incipient carcinoma, where there is a hypochromatosis and atypical mitosis with irregularity of position and relationship of one cell to another and also in size.

DR. SCHOCHET said in closing that it was impossible to answer all of the questions as we do not possess exact and definite knowledge of the mechanism of cell growth, namely, the factors that cause cells to increase in number under normal physiologic conditions. Dr. Ewing has emphasized many basic problems on growth pertinent to this work. At the present time it is not possible to

determine whether we are increasing the longevity of life of these endometrial cells. We are not aware of the length of life of most of the cells of the body with the exception of the nerve cells (which do not reproduce) and the non-nucleated red blood cells which are believed to live between twenty-one and twenty-four days in the blood stream.

In reference to the transplants there is an increase in the size, structure, and arrangement of the endometrial glands. Many mitotic figures are present, and on this strong presumptive evidence one may conclude that there is an actual increase in number (hyperplasia) of cells. It is not possible, however, to ascertain whether the cells present are from the original transplant plus hyperplasia, or only the progeny of the absorbed endometrial cell transplant. In one animal, Case 4, this transplant was active after a period of nine months, and it is extremely doubtful if active normal endometrial cells live for this long period of time, since in situ, they are replaced during each diestral cycle.

Dr. Jacobson's question of virulence of tissue cells requires further elucidation. We are aware of a few phases of viability of cells, but it is desirable to be extremely cautious in adding new theories in our present state of knowledge of the individual cell. In the infections due to plans (bacteria) and to animal parasites (protozoa) there is a difference in the reactions to these groups in the animal body, but whether this analogous condition exists in the tumor cell or in the normal cell remains an academic question. It is conceded that every cell retains its inherent potential power to reproduce within certain limits, with the exception of nerve cells, when stimulated to growth by irritation or weak toxins.

Detail analysis of the work of Dr. Frank on lipoid extracts were omitted in the outline of Dr. Schochet's experiments as this work is based on an entirely different principle. The suggestion of Dr. Frank of the action of hormones on the vascular reactions of the transplants may prove to be a very interesting experiment. In Dr. Schochet's experiments a modification of Loeb's idea of artificial parthenogenesis of the eggs of sea urchin, etc., was attempted with endometrial cells after a primary sensitization. Too little study has been given to the detail and minute structure of the cell. Further studies of the mitochondria, Golgi apparatus, internal changes of the cell during the cyclic period is required.

THE OBSTETRICAL SOCIETY OF PHILADELPHIA

MEETING OF NOVEMBER 3, 1927

Dr. Edward D. Atlee (by invitation) read a paper entitled **Preliminary Report on Treatment of Congenital Lues.** (Published elsewhere.)

Dr. Owen J. Toland (by invitation), read a paper entitled **Some Factors in Postpartum Maternal Morbidity.** (For original paper see page 411.)

DISCUSSION

DR. EDWARD A. SCHUMANN considered that the standard of morbidity as laid down by Dr. Toland was an extremely exacting one. A temperature reaching 100° twice in any twenty-four hours is a standard which would tax the skill of any obstetrician to maintain. In all the causes mentioned morbidities would apparently occur most often in puerperal endometritis with absorption of bacterial toxins which we call sapremia, and which is the commonest cause for elevation of temperature.

As to lochial block, Dr. Schumann felt that lochial block means nothing but a cessation of lochia. The hospital from which the statistics are gathered is to be praised for the very low morbidity shown.

DR. EDMUND B. PIPER wanted to call attention to the fact that in the terminology employed in this hospital the term lochial block is used to cover sapremia. The temperatures were taken every four hours over a period of four days and the morbidity included follicular tonsillitis.

DR. JOHN C. HIRST, II, said that as regards lochial block, it would be interesting to know how many cases were primiparous individuals and how many multiparous.

DR. MONTGOMERY said that in the Department of Obstetrics of the Jefferson Medical College, the standard of morbidity is a temperature which reaches 100.4° twice in one day or on two successive days, not including the first twenty-four hours after delivery. The morbidity at this hospital has been running about 25 per cent. This ratio would probably be a little higher under the standard Dr. Toland has given. However, he included the temperature reaction after cesarean section and of a number of cases of vaccinia, the reaction of the vaccination happening to occur during the puerperal period. Probably in the final analysis, the figures would be about the same.

DR. CLIFFORD B. LULL read a paper entitled **Cesarean Section—A Review of 109 Cases.** (For original article see page 403.)

DISCUSSION

DR. STEPHEN E. TRACY said that in a study of 1001 labor cases at the Jewish Maternity Hospital, 47 had pronounced advanced cardiac lesions. The treatment consisted of absolute rest in bed for several weeks before delivery and such medication as was necessary. The patients were allowed to go into natural labor. Morphia and scopolamine or morphia and magnesium sulphate were given during the period of dilatation. At the end of the first stage of labor under light anesthesia, 12 had normal deliveries, 34 were delivered with forceps and 1 was delivered by podalic version. In these 47 cases there was one maternal death which occurred in a patient with pronounced mitral stenosis with double pneumonia. This patient went into labor prematurely.

DR. CHARLES MAZER wanted to make a plea for the low cervical cesarean section which gives a much lower mortality. It is especially indicated in the potentially infected cases. Dr. Mazer had done only half the number of cesareans reported by Dr. Lull, but all with the exception of two were low cervical cesareans. Every patient had a good test of labor; some had forceps applied at home by their family physician. One primipara, thirty-six years old, was in labor thirty-six hours and was very toxic. A low cervical cesarean under spinal anesthesia resulted in a complete recovery after a prolonged convalescence. A low cervical cesarean is a little more difficult for the beginner and takes a little longer to do, but it is the safest operation giving the lowest mortality in the hands of the average surgeon. Dr. DeLee reported 350 cases with a mortality of only three. Dr. Mazer's series yielded no mortality. It seems to him that a woman who has had a cesarean deserves a test of labor in her subsequent pregnancies. Many of them deliver themselves spontaneously or with the aid of low forceps.

DR. DANIEL LONGAKER believed in the need for a clear definition of the test of labor and no woman has really had the test of labor unless that test is actual labor. If the patient has been in labor eight, ten or twelve hours, or even longer,

and it is the first stage, that is not a test of labor. He thinks the case to which the preceding speaker referred well illustrates the point. That woman had been in labor a number of hours, but when it came to actual labor, it did not take her very long to put it across. He differed with the last speaker and would urge not to bank too much upon immunity from morbidity or mortality in the low operation in a potentially infected case; under these circumstances there will surely be a rude awakening and disappointment will follow. Moreover, it is not always a safe operation. Dr. Harriman, his associate, has had his lesson: the low operation in a woman who had actually had a number of hours of the test of labor, the head firmly inpacted at the brim in which craniotomy would better have been done because the woman was actually infected and died. In this case it required strong forceps traction to disengage the fetal head upwards and the child was stillborn.

Finally there is this question of local anesthesia, and here he felt there was one method of anesthetizing these patients extremely valuable especially in the toxemia cases and that is spinal anesthesia. It is very practical and safe so far as any method of anesthesia can be safe. Regarding the cardiac cases and the choice of ether, Dr. Longaker did not agree that ether is the safest of the inhalation anesthetics in obstetric cases. Following the lead of the late Sir James MacKenzie he would make a plea for chloroform in these cases. Here is one to whose counsel we should listen with very great respect for he was not only cardiologist but also general practitioner and obstetrician. MacKenzie's dictum as to the safety of this anesthetic in these cases should never be forgotten. "I always gave my obstetric patients in labor chloroform—my cardiac cases—and it never hurt them," says MacKenzie, and his words are worth remembering. Dr. Longaker said that his own rather large experience amply confirmed their truth.

DR. EDWARD A. SCHUMANN felt that one thing should be brought to the attention of the profession more earnestly, namely the basis upon which mortality rates are computed. Some believe that cesarean section in elective cases offers safe and nontraumatic way of delivery even in women who might be delivered by the vaginal route. When we are faced by mortality from clinics, the operation assumes a formidable aspect which is purely relative and not true of the case. Dr. Schumann believed we should go back to the old division of cases of cesarean by election and of necessity. Obviously rupture of uterus, separation of placenta—these cases ought not be grouped with the elective cesarean where the abdominal route has been chosen as the least traumatic method of delivery.

DR. LULL (in closing) said he had no intention to start an argument in regard to low cervical section. One hundred and three of those cases were operated upon with membranes intact. The low cervical section is technically a more difficult operation, and although it has a definite place in obstetrical surgery, Dr. Lull saw no reason for doing it in any of this series. In answer to Dr. Tracy, the two cardiac cases included in this group had very definitely impaired hearts. If he included all the women who had cardiac diseases he should probably include 25 or 30. All of the cases who had had previous section were done for contracted pelvis. In answer to Dr. Longaker, Dr. Lull assured him that when he said "test labor," he meant several hours of good vigorous uterine contractions.

The question of local or spinal anesthesia is very important. Personally he preferred to use local anesthesia, and although he had only done 15 cesareans with novocaine, he liked it very much. In only two cases was it necessary to give gas at the time of the extraction of the child. He agreed with Dr. Schumann, that it would be unfair to compare the statistics of this series with a series where they had a different class of cases. However, this report included all the cases done at the Lying-In Hospital during the past thirty-six months.

THE CHICAGO GYNECOLOGICAL SOCIETY

MEETING OF MAY 18, 1928

DR. A. E. KANTOR demonstrated a tumor resembling a dermoid cyst which was removed from a fifty-one-year-old patient whose menopause occurred three years before.

The main complaint was pain in the pelvis on standing. Examination showed a hard tumor mass lying in the pelvis on the right side attached to the vaginal wall. She was brought to the hospital, and through a vaginal incision the tumor was removed. It proved to be a calcareous ovary; the contents of which were a gelatinous mass, somewhat resembling a dermoid cyst. It did not contain any of the thick material usually found. There was no other ovary. She made an uneventful recovery. On a recent examination she stated she was free from pain. The histologist could not definitely determine the type of cyst, but it was very likely a calcified corpus luteum cyst.

DR. R. A. SCOTT presented a paper entitled **Hemiplegia During Pregnancy, With the Report of a Case.** (For original article see page 401.)

DR. RALPH A. REIS (by invitation) presented a paper entitled **A Comparative Study Based on Five Hundred Consecutive Cases of Induction of Labor.** (For original article see page 392.)

DISCUSSION

DR. W. C. DANFORTH said that with reference to the use of quinine he thought that some of the poor results and the loss of fetal life were due to the fact that the doses in some instances are far larger than in the series reported. In his work he does not use over ten grains, two doses of five grains each at an interval of one hour. Many times much larger doses have been used, and they may have had something to do with the mortality that has been reported.

In choosing cases for induction by the Watson method of castor oil and quinine, one should determine by rectal examination in the office whether the patient is ready to go into labor. If the os will admit the finger, Dr. Danforth thought the chances were better than if one is dealing with a closed cervix, and furthermore the trauma required to enter such a cervix is far less. The essayist brought out the point that any method of induction has morbidity connected with it because the cervix is not clean, or free from bacteria, and the morbidity increases with the amount of interference. Stretching gives a little more morbidity than the use of drugs alone. The morbidity which comes from induction with the bag is greater than from mere stretching, because the trauma is greater since a foreign body remains in for hours. Dr. Danforth has had the same experience as the essayist and his colleagues. His mortality in forty-eight bag inductions was about 12.5 per cent. The patients are febrile for a time. The essayist's morbidity after stretching was 6 per cent in one series and 8 per cent in another, which proves that there is a certain definite morbidity to be looked for when these things are done. In the series reported it can be assumed that there was a definite indication in each instance.

Dr. Danforth, referring to the statement that primiparae responded as well as multiparae, said his impression was that the multipara responded a little better. In his work he has come to use the method by castor oil and quinine, pituitrin, and

stretching practically to the exclusion of the induction with the bag, for the reason that the morbidity in the latter is definitely greater, as his experience and that of the essayist have shown. Where the method is used carefully and no undue trauma is used in stretching and the patient is kept under careful observation after giving the pituitrin, there is not much danger. In his work he used 3 minims at a time at intervals of thirty minutes, the second and third doses not being given if the pains come on. He considered the method a very safe one that can be used in hospital work with a high degree of confidence.

DR. N. S. HEANEY said he was particularly pleased that the only methods of induction of labor which the essayist used were castor oil and quinine or the bag only if mechanical means became necessary. He believed that no other methods for the induction of labor need be considered at the present time. Rectal tubes, bougies and bags should be frowned upon.

Dr. Heaney had never seen a case where he thought that the quinine had any bad effect on the fetus. He never used more than nine grains of quinine at one time, giving three grains every hour for three doses, and if pains started the whole dose need not be given. Careful inquiry is made to see whether the patient has any idiosyncrasy for quinine before the first dose is given, because this is a very common peculiarity.

DR. RUDOLPH W. HOLMES said that for many years he had been convinced that bag induction was a mistake, as was the catheter, for induction of labor in minor pelvic deformities; for, if there should be an error of judgment in any individual case and after labor had supervened it was found that there still was cephalopelvic disproportion, cesarean section would have to be ruled out. As two bodies cannot occupy the same space at the same time, there is always a displacement of the presenting part with bag induction with a resultant high incidence of compound presentations or abnormal positions produced by the method. Anyone who minimizes this fact is stating an untruth. For years Dr. Holmes reserved the bag for previas, or other indications where urgency is a real element. He has frequently used the blind catheter for induction and always with success, even though there was a greater frequency of failure the first time than with the bag, and most certainly it was slower in action.

Dr. Holmes employed quinine, castor oil and pituitrin for years. He had used nasal applications of pituitrin on the personal suggestion of Dr. Hofbauer. He did not believe the results with nasal application could quite compare with the repeated small hypodermic injections of pituitrin. He cannot reconcile the statement that quinine has a pernicious effect on the baby for in the South physicians do not hesitate to exhibit large doses, seventy-five grains and more, with no ill-effects to mother or baby, in the presence of malaria. His custom was to give five grains hourly, for five or six doses, stopping with tinnitus, along with the oil and pituitrin.

The day before this meeting Dr. Holmes had tried a new method, new at least in this country, the induction of labor by the use of thymophisin. Twenty minutes after the first nasal application the patient had strong active labor, but after the second dose, an hour after the first, pains ceased, so that the next day the procedure had to be repeated. Apparently thymophisin does have a more definite action than pituitary extract, whether it really is better than the latter has yet to be proved.

He believed it was a serious mistake to use bag or catheter induction, or even to stretch the os, for each method carries with it risks which certainly will compromise the patient in the event that a section were required.

He asked Dr. Reis what happened to the other six per cent of the bag inductions, for he gives data on only 94 per cent.

DR. C. B. REED said he first called attention to the induction of labor at term in a paper before the American Gynecological Society in which he reported a series of three hundred bag inductions. He thought Dr. Reis would be interested in comparing the opposition which this paper encountered with the generous reception accorded his own work.

Dr. Reed was gratified to perceive and report that in the fifteen years which had elapsed since the publication of his paper the induction of labor at term had become a definitely established operation. The literature no longer teemed with queries and uncertainties regarding the employment of the maneuver but rather like the present essay what form or method would best succeed.

Dr. Reed reported that he had continued his investigations at intervals and used various methods. He reported 421 cases of pure castor oil and quinine induction, 383 cases of bag induction, 218 of pituitrin by injection and eight by nasal application. He also thought several patients had gone into labor through oral administration of pituitrin though he could not be sure.

His observations agreed with those of the essayist in the equality of responsiveness between multiparas and primiparas. He thought also that while castor oil and quinine would succeed in about 60 per cent of the cases yet the bag remained as the most reliable of the mechanical measures.

Dr. Reed's opinion regarding the stripping of the cervix which he expressed in the discussion on his paper in 1913 was unchanged. He still believed that the finger could not be introduced without carrying contamination from the vaginal walls into the cervix. The bag on the contrary being passed by sight and without contacts will enter clean. This point is supported and proved by the essayist in his morbidity report.

The question of pituitrin induction was most important. Many obstetricians have declaimed against the use of the drug and yet Dr. Reed, with an experience of 9,000 or ten thousand labors wherein pituitrin has been exhibited under his supervision, has not found a single instance where the disability of mother or child could be logically attributed to the drug. He regarded this agent as a powerful adjuvant to the obstetrician; though it was, like strychnine, morphine, antitoxin or even the knife, capable of misuse. Danger and damage can result from any drug which is ignorantly employed, and it is always well for those who do not understand the dosage or technic of administration to avoid the use of pituitrin altogether. The inexperienced should not decry a method or agent which they are afraid to use. The good surgeon does not denounce the knife.

Dr. Reed agreed with all the essayist's conclusions except the stripping of the membranes. He wished particularly to note and emphasize the finding that the introduction of the bag did not disturb the presentation. Dr. Reed made this point in his first paper but the charge has been thoughtlessly repeated again and again. The disturbance of the presenting part is almost entirely a matter of technic. The bag is intended for introduction into the cervix where it is harmless; but if an attempt is made through ignorance or design to carry it to the fundus, the presenting part may suffer dislocation.

Dr. Reed was disposed to criticize the use of the terms mature and postmature. How did the essayist estimate his time? Was he so fortunate in the selection of his patients that they could give him all the necessary data? Many women frequent the obstetric clinics who have four or five babies without a menstrual flow. How did Dr. Reis manage such conditions? Did he measure the uterus or child? Dr. Reed thought it was very unwise for obstetricians to deprive themselves of the advantages which follow the routine measurement of the intrauterine

child. From these maneuvers the maturity of the child can be readily assured and other fetal conditions clearly and comprehensively determined. The McDonald, Ahlfeld and Stone-Perret methods were not difficult to acquire.

DR. MARK GOLDSTINE said that the most favorable time for the induction of labor is at term. The most favorable patient is a normal obstetric case. In his opinion the difficult time to induce labor is from the twenty-fourth to the thirty-second week. That presents an entirely different problem, particularly if one is faced with some severe pathologic condition such as severe toxemia or abruptio placentae. In placenta previa, quinine and castor oil are the wrong treatment because the more severe the pains, the greater the hemorrhage, until some means of checking the bleeding have been instituted.

As to inducing labor at term in normal pregnancies that is a matter of personal opinion. He has had difficulty in inducing labor around the seventh month when a difficult problem was at hand. He has never found any one method that was seventy-five per cent or eighty per cent good. He has had cases where castor oil and pituitrin did not work, where bag induction did not work, and where the bag pulled out of the cervix and left it undilated.

DR. CAREY CULBERTSON said that as a general proposition castor oil and quinine in his experience has been so satisfactory that he uses it first and only when it fails does he resort to one of the other methods. The rubber bag induction seemed to him to need a little further analysis. In some clinics the induction is started with a small bag, such as the old Carl Braun bag, then larger ones are inserted as the cervix dilates. He believed that this was an added factor in the sustained morbidity. For that reason he never uses a small bag but always a large one, such as the Voorhees' or de Ribes'.

The fetal morbidity following these labor inductions, as was pointed out, is of first importance. He had seen only one case, and that last year, where he believed the death of the child in utero might be attributed to the quinine; though he was neither persuaded nor convinced that that was the cause.

He asked Dr. Reis where attempted induction fails, how long does he wait before making another attempt? It has been his practice not to repeat the attempt at induction for several days, usually three, where it has not been effective the first time, provided the condition is such as to make it possible to wait. He referred, however, to patients who are at term and where labor is being induced on that indication.

He thought the point brought out by Dr. Goldstine with reference to the induction of labor in pathologic conditions prior to term was very well taken. Those are the cases that are the most difficult to put into labor; and where induction fails by one of these methods, it becomes necessary to attack the problem along entirely different lines.

DR. IRVING F. STEIN said he would like to correct one impression that Dr. Reis gave, namely, that all maternity cases at Michael Reese Hospital are examined vaginally. That applies to service cases for teaching purposes. In his own work when a patient comes in in labor she is not examined vaginally.

The question of stretching brings up a point that Dr. Danforth emphasized. He felt that if the lower segment is formed almost any method would succeed in inducing labor. If stretching alone was done, labor would set in. He has frequently seen patients who come in for examination with the cervix effaced and simple stretching would send the patient promptly into labor, particularly in multiparae. There are cases where the membranes rupture without examination. Rectal examinations show that membranes rupture, the cervix effaces and the patient goes into labor. In a comparison of those cases that are stretched without the use of quinine

and castor oil with those in which the drug was given, he stated that years ago quinine was used quite routinely, but it was observed that the heart tones became irregular, and the meconium discharge was more frequent than where quinine was not used. Not more than one minim of pituitrin is used because some patients have violent reactions from a three minim dose.

When the cervix is not effaced, the induction of labor by the ordinary bag produces crampy pains which do not dilate the cervix. This really constitutes a failure of induction. Sometimes eighteen to twenty-four hours later the patient goes into labor without an additional method being employed. Dr. Stein placed a twelve hour limit on the bag. He had such an experience in a multipara where simply crampy pains resulted. A leakage occurred in tying the tube and after six hours the bag came away. The pains continued as crampy pains. Not until twenty-four hours later did any change in the cervix present itself. The patient required a sedative in the meantime. She then went into labor and delivered spontaneously.

DR. H. W. SHUTTER of Milwaukee asked if Dr. Reis had any other means of inducing labor in the toxemias that could compare in efficacy to the bag.

DR. C. D. HAUCH said it had been his privilege since the beginning of Dr. Reed's induction work at Wesley Memorial Hospital not only to observe but also to deliver patients himself. The valuation that is placed on any type of work or any method will depend upon the results which that method produces. The mortality and morbidity rates will decide its merits. At Wesley Memorial Hospital the infant mortality rate in 1927 was fourteen per thousand. He was sure that the work of Dr. Reed and others practicing induction at Wesley did not tend to raise that percentage. In hospitals where these methods are not known or used the mortality rate in infants has been as high as seventy-nine per thousand, according to the statistics of the health department.

DR. J. P. GREENHILL said in discussing the effect of quinine on the fetus and the mother that it might be of interest to know that some specimens of quinine contain histamin. Hofbauer experimenting in animals produced abruptio placentae and a condition similar to eclampsia by injecting histamin. Perhaps some of the severe cramp pains and some of the fetal deaths therefore may be attributed to the histamin present in some specimens of quinine.

DR. REIS in closing said in answer to Dr. Danforth's question about the state of the cervix, that there was a slight difference when the cervix was effaced. Twenty-seven per cent of the successful inductions were in patients in whom the cervix was partially or completely effaced. In the unsuccessful group there were eighteen per cent who showed partial or complete effacement, so that effacement does favor a successful induction.

He had a separate series of twenty-six patients in whom stripping was done without any medicinal induction. Of the twenty-six, fourteen responded immediately by going into labor—something between fifty-five and sixty per cent.

In answer to Dr. Heaney's query about the dose of quinine, he said that in this series it was used in five grain doses repeated hourly for a maximum of three doses, so that the total quinine the patient received amounted to fifteen grains.

In reply to Dr. Holmes's question as to the discrepancy in the figures for bag induction, he said the six per cent that did not respond represented one of the thirty-eight patients. In that patient the cervix dilated to about 4½ cm., the bag came out and the pains stopped. She was left undisturbed for forty-eight hours, and then labor was induced with castor oil, quinine and pituitrin. That has been regarded as a bag failure and is the only one. Of course, only thirty-seven patients delivered.

With the bags Dr. Reed uses castor oil, castor oil and quinine, and some pituitrin. In this series care was taken not to mix the different types of induction. In thirty-eight patients the bag was used alone, and nothing was given in the way of medication to stimulate labor pains.

Dr. Scott asked about the dose of pituitrin. One patient in this series after the second dose of pituitrin showed a mild uterine tetany which lasted about thirty minutes. She was a twenty-seven year old primipara, apparently at term. The cervix was not stretched. She was simply given one minim of pituitrin and following the second minim developed severe lower abdominal pain; the uterus immediately contracted and remained contracted for about thirty minutes. If that result can occur from one minim doses, he would be afraid of three minim doses. The patients made no comment as to discomfort from the number of hypodermics they received.

The bags used in this series were of the larger type of Voorhees' bags. None of the small Carl Braun bags were used. If the first induction was unsuccessful, nothing was done to the patient for forty-eight hours. After that a second induction was attempted. Some were allowed to go over seventy-two hours, but in none was the interval between the first and second injection as long as one week, to which Dr. Culbertson referred.

Dr. Goldstine and Dr. Shutter referred to cases of induction in patients who were not near term. That type of patient was not considered in this series. This study was an attempt to compare the methods at the most favorable time, which is at or near term. The favorable results of any method of induction decrease in direct proportion to the degree of prematurity.

DR. A. F. LASH (by invitation) presented a paper on **The Therapeutic Value of a New Concentrated Streptococcus Antitoxin in Puerperal Fever.** (For original article see page 297.)

DISCUSSION

DR. FRED H. FALLS said he felt that the use of antistreptococcic serum in puerperal fever is a step in the right direction in combating this disease. Interest in this has been aroused by the work of Dick and others on scarlet fever and erysipelas. With this type of serum a result can be expected that is comparable to the effect obtained in scarlet fever and erysipelas rather than the type of reaction that has been observed in diphtheria.

The toxin of streptococcus is not a pure exotoxin but is both an exotoxin and endotoxin. It is important, as Lash has been able to show, that these toxins produce exotoxins and that he can produce serum that will neutralize this exotoxin. Another important thing to be stressed is that to be of any value the serum must be administered early. Too often in cases of puerperal sepsis everything else is tried and then when it becomes apparent that the patient is moribund, a frenzied attempt is made to inject every and all kinds of serum that may as a last resort do good. This is not the way to treat these infections. The results, as Dr. Lash has shown, are secured when the diagnosis is endometritis or myometritis. The fact that in these cases he was able to reduce the mortality to about five per cent substantiates this statement. Nobody knows what would have occurred in these injected cases if he had not injected the serum. Everyone has seen patients with streptococcic infection who have gotten well spontaneously, and likewise, there are cases in which streptococci were present in the cervix following delivery and no fever occurred. Therefore, the difficulties of arriving at conclusions in these cases are apparent to anyone who has done this type of work. Only by carefully controlled statistics can conclusions be drawn.

The advantage one has in using antistreptococci serum in puerperal sepsis is that one knows fairly definitely when the disease starts, in the sense that if one has a patient who has had a difficult forceps delivery, a manual removal of the placenta, and the next day develops fever, he can immediately make a smear and culture from the vagina and within a few hours arrive at a diagnosis and use the serum. That is the way serum should be used.

The diagnosis is usually relatively easy in puerperal sepsis as compared with scarlet fever. Pyelitis, breast abscesses, and other causes of postpartum temperature can usually be ruled out easily. The characteristic findings, physical and bacteriologic, in the pelvis clinch the diagnosis. Another advantage as compared with erysipelas is that one is dealing with young individuals not with older people who so often succumb to streptococcic infection. A disadvantage is that one is dealing with individuals who may have had severe hemorrhage.

Further work must be done. He felt that the next step in this type of work should be the taking of alternate cases, so that the results could be compared in the cases in which serum was given and those in which it was not.

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

New Books

BY ROBERT T. FRANK, A.M., M.D., F.A.C.S., NEW YORK CITY, N. Y.

OF GENERAL INTEREST

TWO entirely nonmedical books have struck me most favorably. They should interest both the medical and lay reader. The first one dealing with adolescence is surprisingly fascinating, and I refused to lay it aside until I had read it from cover to cover. The second book to be discussed contains a fund of interesting information and is charmingly written.

Coming of Age in Samoa[1] is a psychologic study of primitive youth for the benefit of western civilization. This investigation was performed by Margaret Mead, assistant curator of ethnology in the American Museum of Natural History.

Franz Boas who wrote the introduction, says that up to this time hardly any one had taken the pains to identify himself sufficiently with a primitive population to obtain a real insight into its problems. Miss Mead did undertake to identify herself so completely with Samoan youth that she is able to give a lucid picture of the joys and problems of individuals in a culture different from our own. The author is really interested in determining whether the rebellion against authority, the philosophical perplexities, the flowering of idealism, the conflict and struggle so characteristic of our present adolescents were due to the difficulties inherent to adolescence or resultant from being adolescent in America.

As the test colony of Herodotus in which babies were to be isolated and the results recorded is not a possible approach, an anthropologist is forced to go to an entirely different civilization and make a study of its problems under entirely different cultural conditions. She therefore chose a primitive group whose language does not possess our Indo-European categories, whose religious ideals are of a different nature, and whose social organization is not only simpler but very different from our own.

Her study is based upon the adolescent girls in Samoa, and of these she chose all the girls in three little villages on the coast of the little island of Tau. Nine months were spent in Samoa and fifty girls were studied.

It is really difficult to summarize this most interesting book which reads like a novel. These Samoan girls were traced from babyhood through their task of baby tending and their instruction in the making of the oven, the weaving of fine mats, and the forsaking of the gang of children, to become members of the household. The Samoan girl defers marriage through as many years of casual love making and sex

[1] **Coming of Age in Samoa.** By Margaret Mead. William Morrow & Co., New York, 1928.

experience as possible, but she finally marries and settles down to rear children who in turn will repeat the same cycle. In Samoa growing up is easy and simple, a part of the general casualness of the whole society. No one plays for very high stakes and no one pays very heavy prices. Disagreements between parent and child are settled by the child moving across the street. Occasionally misfits and delinquents are encountered. Sex is a natural, pleasurable thing. The freedom with which it may be indulged in is limited by just one consideration, social status. Chiefs' daughters and chiefs' wives should indulge in no extra-marital experiments. Samoan civilization discounts strong feeling and its primitive civilization favors tranquillity. In addition there is an almost entire lack of neuroses among Samoans. Difficult situations rarely arise. A low grade moron would not be greatly handicapped in Samoa where the range of variation is small. There is no close relationship between parent and child on the island, and there is a resultant lack of specialized feeling. In other words the home does not dominate and distort the life of the growing child. This lack of specializing of feeling applies also to the sex feeling. No reticence is encountered. The Samoan child sees intercourse, pregnancy, childbirth and death as familiar occurrences.

From the time that Samoan children are four or five years old, they perform definite tasks graded to their strength and intelligence. This does not mean that they have less time for playing than American children. Their tasks have a direct application to adult life, quite different from those of our children. The most characteristic of Samoan traits is the laissez faire attitude toward children.

The author says that realizing our own ways are not humanly inevitable nor God ordained but the fruit of a long and turbulent history, we may well examine in turn all of our institutions, thrown into strong relief against the history of other civilizations, and weighing them in the balance, be not afraid to find them wanting. Samoa knows but one way of life and teaches it to her children. Will we, who have the knowledge of many ways, leave our children free to choose among them?

Folklore of the Teeth by Leo Kanner[2] is a most interesting, well written and stimulating monograph. It is of interest to the historian, the student of folklore and the medical man as well as to the ordinary lay reader. The book is well written and replete with many types of information.

Aristotle thought that men had more teeth than women. Christoph of the golden tooth, who pretended in the 16th century to have acquired this golden appendage through a miracle, shows some of the charlantry connected with ignorance and credulity. Aids to dentition include the Frankonian remedy of biting off the head of a living mouse, the head then being worn in a linen bag. In many localities shed milk teeth are carefully stowed in a mouse hole in order to aid the growth of the permanent teeth.

The hygiene of the teeth has been a subject of importance throughout the ages. "A diamond is not as precious as a tooth" says Cervantes. Every race has prized good teeth. Chewing for the sake of dental hygiene accounts for the use of mastic, betel, and gambin. (I wonder whether our national habit of gum chewing can be placed

[2]**Folklore of the Teeth.** By L. Kanner. Macmillan Co. New York, 1928.

upon any such useful and excusable basis.) Toothpicks have been found among Hallstattian relics. Among the primitive tribes the siwak may be regarded as the precursor of the toothbrush, the palm stem or similar fragment being used to clean the teeth.

Toothache is generally recognized as one of the worst pains to which mankind is liable. Therefore amulets and charms abound. Kanner mentions with comment 133 plants which have been prescribed by primitive and civilized nations for the cure of toothaches. St. Appolonia throughout the ages has been recognized as the patron saint of toothaches. She suffered her martyrdom 248 A.D. and underwent extraction, pulling, knocking out and mutilation of her teeth and jaws. Among savage tribes transference of toothache, most commonly to some inanimate object such as a tree, is still practiced. Although the Egyptians have been credited with the utilization of false teeth, no mummies substantiating this claim have ever been found. The ancient Romans, however, used false teeth more than 500 B.C. Deformation of the teeth by pointing, filing, and removal are practiced by many savage tribes. Staining of the teeth is also a common practice among them. Primitive as well as savage nations have used teeth as ornaments, as charms and as jewelry.

This scholarly and instructive book is to be highly recommended to all readers interested in history, folklore and customs.

GYNECOLOGY

The fourth edition of Graves' *Gynecology*[3] shows a large amount of work expended on this revision and rewriting. This book is large for a medical school textbook but contains a tremendous amount of general and detailed information. In order to make it more accessible to the medical student, Dr. Graves has concentrated the information most important for the third and fourth year student in Part 2, which covers gynecologic disease and is about 500 pages in length.

In the huge amount of such material, only a few high spots can be referred to in this review. In spite of, or perhaps because of, so much minute detail in the chapters on menstruation and ovulation, the average reader will be somewhat confused although I have found many well worth-while points discussed by the author. I would suggest that in the next revision the main theme be brought out with greater clarity, that much of the historical deadwood be removed and that less attempt at giving the entire world's literature be made. Few textbooks will equal the clearness and detail with which carcinoma of the cervix, adenocarcinoma of the fundus, and the radium treatment of carcinoma are taken up. Considerable space is given to the lead treatment of cancer. I know of no textbook in which the discussion of endometrioma and endometriosis is more complete. This same praise applies to the chapter on sterility. The technic of the application of radium to the cervix is carefully given and well illustrated.

The large section dealing with operative technic shows a few but not very important changes and additions. I see that the Schubert operation for absence of the vagina has been added. I hope that the next edition will illustrate the Frank-Geist technic by means of the tube flap which has now proved itself of real value in our work and

[3]**Gynecology.** By W. P. Graves. Ed. 4. W. B. Saunders Co., Philadelphia, 1928.

which is devoid of all risks which accompany both the Schubert and Baldwin technics. If ever the book requires diminishing of material, I would suggest that the chapters on kidney and rectal operations be omitted and that the portions dealing with the relation of gynecology to the general organism be abbreviated.

I have read this book with a great deal of care and interest and therefore do not hesitate to praise its good points and to point out possible means of improvement. For example, it seems that Figs. 63, 64, and 69, dealing with chronic endocervicitis are unmeaning, and this same applies to Fig. 141 of hydatid mole. Some criticism of other microscopic figures could be made. This does not apply to the excellent gross illustrations made by the author.

All in all, this is one of the best textbooks in any language.

The huge *Biology and Pathology of Woman* by Halban and Seitz[4] is nearing completion. Only the chapters on "Vitamines" and "Fever During Pregnancy" remain to be published, together with the vital volume containing the complete index. Forty-four separate installments have so far appeared, and it is with the last two, numbers 43 and 44 that I have to deal now.

Hoehne has written on ectopic pregnancy. His discussion covers more than 200 pages and while adequate and complete, adds nothing whatever to our present knowledge of the condition. This is, after all, not surprising, as so much study and such frequent opportunities for clinical investigation are offered by extrauterine pregnancy that clinicians have fully exploited this field. The illustrations used in the great majority are taken from Werth who wrote the chapter on extrauterine pregnancy in the *Handbuch der Geburtshilfe* by von Winckel.

In this same installment are a few pages which complete the article of the late Dr. Hitschmann on malignant chorioepithelioma.

The forty-fourth installment contains an article by J. Fischer dealing with the history of medicine during the 19th century in relation to gynecology and obstetrics. The author has taken up each branch of our specialty, for example, discussing the anatomy and embryology of the female sex organs, the physiology of the genital system, the physiology during pregnancy and of the puerperium in turn. This naturally presents the subject in a somewhat detached and fragmentary fashion but permits the author to do justice to a larger number of investigators and authors than would have been possible if he had tried to give a cross-section of only the most striking achievements. On the whole one feels that Fischer has dealt with care and with as great an impartiality as is possible with the medical history of the last century.

An appendix containing the following articles appears with this same installment: The reticuloendothelial system by Robert Benda, pathogenesis of functional disturbances in the female genital system, that is the pathogenesis of psychoneurosis by Walthard, in which the average reader will have some difficulty in following the text because of the special nomenclature which has arisen in this type of investigation; and finally the new discoveries in the interrelationship between hypophysis and the genital system by K. Erhardt.

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[4]**Biologie und Pathologie des Weibes.** Herausgegeben von J. Halban und L. Seitz. Urban & Schwarzenberg, Berlin, 1928.

The clinical lectures on *Tropical Gynaecology*[5] by Green-Armytage contain some extremely interesting chapters. These lectures cover the author's own experience during eighteen years and might better be called oriental gynecology. Of especial interest are Lecture I dealing with obstetrics and gynecology in the days of the patriarchs, in which a close scrutiny of the Bible has been made, and Lecture II on obstetrics and gynecology in the East, in which the special conditions confronting the practitioner in India are emphasized.

Tetany and osteomalacia are common. Although the infant weight averages 20 per cent below that of the European (5¾ pounds) high craniotomy, embryotomy, and decapitation often have to be done. Fibroids and tumors of all kinds are first seen when they have reached enormous size. Prolapse of the uterus is extremely common. Vesicovaginal fistula likewise is frequent and of such intractable type that only in 62 per cent of the cases can any hope of cure be looked forward to.

Lecture III dealing with disorders of menstruation is extremely fanciful. In sterility the Hobb's treatment, something new to me, namely, the introduction of glycerine into the uterus to promote exosmosis from the endometrium, is discussed. A good chapter is devoted to the use and abuse of the pessary. Another chapter deals with the operative and nonoperative treatment of prolapse. The author's reflections on "gynaecology" are interesting and show wide reading. On the whole this little book contains much good sense and experience, presented in a most attractive fashion. It is well worth reading and shows the disadvantages under which medical men must labor in backward communities, and how these disadvantages can often be overcome by special aptitude and effort.

Trauma and Compensation in Obstetric and Gynaecological Cases[6] by Lindsay is a valuable monograph for the occasional medicolegal witness who has no larger treatise available or opportunity to study medicolegal literature.

The main mass of the book is occupied by instructive case histories to which the short introductories form a guide. The main divisions of the book are obstetrics, the neonatus, and gynecology. This monograph is a valuable contribution to obstetric and gynecologic literature.

Seitz has written a concise, clear-cut, well arranged and valuable monograph on *Differential Diagnosis in Gynecology*[7] for the practical series on differential diagnosis edited as vol. v by Honigmann.

The subjects stressed are the personality of the patient, which includes the constitution, the normal or abnormal condition of the internal secretory apparatus, the recognition and evaluation of psychoneurosis, as well as the causes of extragenital diseases. Pain and functional disturbances are taken into consideration, especially disturbances of secretion (fluor and menstruation). Pregnancy is considered in connection with women's diseases, the differential diagnosis, the disturbances of pregnancy, and pregnancy complications being dealt with. Considerable space is devoted to disturbances caused by

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[5]**Tropical Gynaecology (Clinical Lectures).** By V. B. Green-Armytage, M.D. Thacker, Spink & Co., Calcutta and Simla, 1928.

[6]**Trauma and Compensation in Obstetric and Gynaecological Cases.** By D. M. Lindsay. Wm. Hodge & Co. Ltd., Edinburgh and London, 1928.

[7]**Differentialdiagnose in der Frauenheilkunde.** By Dr. Med. A. Seitz. Theodor Steinkopff, Dresden und Leipzig, 1928.

bacteria and parasites. Then the differential diagnosis of neoplasms is discussed. Chapters are devoted to malpositions, malformations, injuries and differentiation of diseases of the genital tract from those of the neighboring structures.

Although the author makes no attempt to deal fully with the literature, there is no excuse for calling Cullen's sign of ectopic pregnancy, the discoloration of the umbilicus, the Hoffstäter-Cullen sign, or to fail to mention Rubin of New York when describing the technic of insufflation. I am also surprised to see that Seitz still features the use of Abderhalden's test for the determination of pregnancy.

Radiologic Investigations in Gynecology by Claude Béclère[8] was crowned by the Academy of Medicine. Among the subjects dealt with are pneumoperitoneum and tubal insufflation of which a bare outline is given, the main emphasis being placed on the injections of opaque substances, especially lipiodol.

A careful résumé of the technic is presented and the succeeding portion of the book is mainly devoted to the results. Numerous and good reproductions of radiograms are given. The concluding chapter is devoted to therapeutic deductions.

On the whole I consider the author's attitude toward lipiodol injections far too radical and that he uses it too frequently for safety. The study is critical and instructive but personally I limit the use of lipiodol for tubal diagnosis to cases where impermeability has been determined by the insufflation method.

Pettinari's large monograph[9] covers the entire subject of *Ovarian Grafts* as well as that of the endocrine action of the ovary. His work was done during three years in Pavia and one year in Paris. Delayed publication has greatly impaired the value of this earnest contribution to endocrine studies as the book appears to have been completed in 1925 and only sees the light of day in 1928. Consequently much of the newer physiology which has appeared since 1925 is not presented in this monograph.

The author says that the graft from monkey to man is still entirely in its experimental stage. More important than similarity of blood groups is the fact that a graft from a youthful woman not from an old one should be utilized. Autoplastic grafting may give remarkable results. In homoplastic grafting only a small percentage of successes can be anticipated. The very valuable contributions contained in this book are obscured by the unwieldy size of the volume.

Horalek has written a monograph on *Salpingitis Isthmica Nodosa*[10] as well as on post-tuberculous adnexal changes. The first 118 pages of the book are written in Tscheckik which I confess that I am unable to read, but the succeeding 60 pages appear in excellent German. The frequent coincidence of tuberculosis followed by salpingitis isthmica nodosa is stressed. The illustrations and the literary references are thorough and illuminating.

Blair Bell has given a short, profusely illustrated brochure covering the activities of the *Gynecological and Obstetrical Department of the*

[8] **L' Exploration Radiologique en Gynecologie.** By C. Béclère. Masson et Cie, Paris, 1928.

[9] **Greffe Ovarienne et Action Endocrine de L'Ovaire.** By Vittorio Pettinari. Gaston Doin & Cie, Paris, 1928.

[10] **Salpingitis Isthmica Nodosa.** Von F. Horalek. F. Topic, Prague, 1928.

University of Liverpool.[11] This department, working in connection with the Royal Infirmary, is a well centralized unit, with modern equipment. The teaching is evidently thoroughly worked up and carefully planned. The department offers for sale over 1100 lantern slides for teachers who are not fortunate in having material at their disposal. Such a department is well able to teach students thoroughly, but too static and fixed teaching equipment and material may lead into a deeply grooved rut entailing the danger of not keeping up with modern advances.

Sterility in Women[12] is limited to diagnosis and treatment. The book is a strictly practical monograph which offers little new to the profession. Forsdike says that the first examination should not be made before twelve months of married life have elapsed; and before serious investigation is undertaken, six months more should pass. This is sane advice. He goes up to 300 mm. of mercury with his air insufflation which, to my mind, appears to be a rather hazardous pressure to exert. He favors lipiodol for examination. Of 41 patients with patent tubes, 14 or 34.4 per cent became pregnant after lipiodol injection. It appears to me this would signify that numerous unnecessary injections had been performed on patients who would have become pregnant without further measures. His therapeutic advice includes nothing new. Three salpingostomy patients became pregnant after opening of the tubes, an unusually large number. On the whole, the attitude of this author is sane and fairly conservative. His outlook, however, is strictly mechanistic, too little attention being paid to other factors which so often influence sterility or fertility.

Technique of Contraception[13] by Cooper should prove a very useful book to the majority of medical men whose training in methods of contraception is notoriously incomplete. Again and again patients complain to me that physicians limit their advice to the phrase "you should take care not to become pregnant" but appear unable to give concrete directions for any but the simplest of contraceptive measures. The text is clear cut, carefully written, and quite objective in some ways but the book is padded and would gain by being greatly reduced in compass.

The author claims to base his experience on five years as director of the Clinical Research Department of the American Birth Control League during which time he had the opportunity of seeing 8000 cases. The indications for giving contraceptive advice are mentioned, but these naturally will have to vary according to the state in which the physician practices. Recognizing this fact, the author has concluded his monograph by an abstract of some of the state laws. The requisites for an ideal contraceptive are correctly given but of course we are not at present in possession of a really ideal technic. Cooper advises a combination of the Ramses pessary with a contraceptive jelly containing 1 per cent lactic acid. His statistics are far from being convincing. Of the 916 cases he uses, at least 456 should be excluded before one can even consider the results, because any time of observation shorter than one year for judging the efficacy of a method is ludicrously inaccurate.

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[11]**The Material and Methods of the Gynaecological and Obstetrical Department in the University of Liverpool.** By W. Blair Bell. Sherratt & Hughes, Manchester, 1928.

[12]**Sterility in Women.** By Sidney Forsdike. H. K. Lewis & Co., London, 1928.

[13]**Technique of Contraception.** By J. F. Cooper. Day-Nichols, New York, 1928.

I wish also that the author had omitted the testimonial-like quotations in chapter one, although I can well understand how he succumbed to the temptation of quoting the opinion of eminent individuals while birth control is being constantly subjected to criticism from so many directions. From the standpoint of value, this monograph is particularly useful as a technical guide to physicians.

Petit-Dutaillis[14] has covered nearly 500 pages with a hodgepodge of loose thinking, credulity, fine writing and erudition. The author loves and delights in diagrammatic circles, clover leaf forms, and other pseudoalchemistic symbols. He has swallowed all endocrinologic nebuli bait, hook and sinker, adorns them, and presents them in extenso. To take a single example, he speaks of "la symbiose endocrino-sympathico-psychique." En passant he objects to modern tendencies in art, sculpture, novels, etc. He quotes repeatedly the text of Bock which deals with "specific corpuscles" secreted by each endocrine gland. In conclusion there is an appendix dealing with a plastic perineal operation, profusely illustrated. For an amputation of the cervix, sixteen separate sutures are employed. In dealing with the anterior vaginal wall and cystocele, the levators are pictured as brought together in front of the cervix while the fasciae are apparently not dealt with. My own impression from the somewhat diagrammatic drawings, is that what the operator really brings together are the fasciae and not the musculature. Books of this kind do no good but produce lots of harm by encouraging loose thinking and wild theorizing.

OBSTETRICS

DeLee's book on *Obstetrics*[15] has reached its fifth edition. As usual, the author has taken great pains in this revision. I cannot fail to agree with DeLee that the very general hospitalization of lying-in women has not decreased either morbidity or mortality in the small towns, because inadequately trained practitioners, encouraged by a false sense of security in hospital surroundings, attempt surgical obstetric procedures which they are incompetent to perform and often interfere when conservative measures are indicated.

The new edition is fully up to its predecessors in completeness, beauty of equipment and careful presentation. The chapter on prenatal care is excellent. The suturing of the placental site during laparotrachelotomy in placenta previa is a new and perhaps useful measure. This operation, that is, laparotrachelotomy, is greatly emphasized by DeLee. He also mentions the Gottschalk-Portes technic of cesarean section with apparent desire to try it out more fully before recommending it without reserve. His enthusiasm for Kielland forceps is extremely small, advising that it would be in the specialist's armamentarium but that the man behind the gun is more important than the type of instrument employed.

The description of menstruation on which so many theories have been advanced, will bear rewriting and clarifying. In the diagnosis of pregnancy by means of laboratory measures, the test of Zondek and Aschheim as well as of Frank and Goldberger might very well have

[14] **Troubles Fonctionnels & Dystrophies en Gynecologie.** By Paul Petit-Dutaillis. Gaston Doin & Cie, Paris, 1928.

[15] **The Principles and Practice of Obstetrics.** By J. B. DeLee. Ed. 5. W. B. Saunders Co., Philadelphia, 1928.

been mentioned as they offer greater certitude than any of those described. The term "dysthyroidism" appears to me a misnomer. If thyroid overaction is meant, it should be so stated. If underfunctioning of the thyroid occurs, this likewise can be specifically so labeled. No one has brought proof that the thyroid secretion alters in its chemical constitution.

The popularity of the *Principles and Practice of Obstetrics* by DeLee is fully deserved. I know of no book of equal compass which is better than this excellent treatise.

In addition to *Tropical Gynecology* previously mentioned in this review, Green-Armytage has issued a second edition of his *Tropical Midwifery.*[16] This small volume consists of lectures for the general practitioner, emphasizing especially those features of midwifery which are peculiar to the tropics. The book is short and paragraphed so as to emphasize and make its contents readily accessible. Osteomalacia apparently is a very common disease in northern India. During the last two years, 26 craniotomies and 15 cesareans were necessitated by this disease in the hospital in which Armytage is connected. He calls attention to the fact that the newborn babies of osteomalacic mothers must be treated for calcium deficiency. In the treatment of puerperal sepsis, which is very common, the author employs antistreptococcus serum, quinine, Fowler's position and fresh air. He advocates more local treatment than we are accustomed to approve of. Every aspect of obstetrics is dealt with, and on the whole this small treatise is an excellent guide, intermediate between quiz-compend and larger textbook.

Another monograph dealing with problems in India is entitled *The Causes of Ante-Natal, Natal and Neo-Natal Mortality of Infants*[17] by A. L. Mudaliar. It embraces two lectures delivered under the Elizabeth Mathai Foundation and concerns itself mainly with the hospital statistics of two large hospitals in Madras where, however, over one-third of the entire births of the city are recorded. Indian birth statistics are notoriously incomplete and unreliable. The author covers the various causes producing neonatal death with a great deal of detail without, however, contributing much new to this portion of the subject. He claims that early maternity (i.e., child mothers), while existing in India, is not as common as is ordinarily supposed. Of 64,000 pregnancies, 2 occurred at the twelfth year, 18 at the thirteenth year, 87 at the fourteenth year and 307 at the fifteenth year. The lectures are attractively written and contain many graphs.

Van Blarcom's *Obstetrical Nursing*[18] has reached a second edition. The book contains a tremendous lot of information, but I am sufficiently old-fashioned to wonder occasionally how much a nurse's usefulness is increased by studying and presumably soon forgetting too much theory during her pupil days. It seems that today overemphasis is placed on book-learning with some consequent neglect of practice.

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[16] **Tropical Midwifery.** By V. B. Green-Armytage. Thacker, Spink & Co., Calcutta, India, 1928.

[17] **The Causes of Ante-Natal, Natal and Neo-Natal Mortality of Infants.** By A. Lakshmanaswami Mudaliar. Associated Printers, Madras, 1928.

[18] **Obstetrical Nursing.** By C. C. Van Blarcom. Ed. 2, revised. The Macmillan Co., New York, 1928.

A Glasgow Manual of Obstetrics,[19] published in 1924, by Cameron, McLellan, Lennie and Hewitt, covers the entire subject in a very complete, clearly planned fashion with the resultant excellent, didactic textbook. The illustrations, mainly in line, resemble those of the classical Faraboeuf and Varnier.

MISCELLANEOUS

Blood and Urine Chemistry[20] by the Gradwohls is a very timely treatise for laboratory workers, technicians, and practitioners of medicine. It deals especially with the blood chemistry methods which are so constantly utilized in gauging the resistance of patients to operation and the traumata of life.

Part 1 deals with the technic of blood chemistry, considerable time being devoted to the colorimeter which is the basis for most of the tests. The concluding chapter of this part deals with alkalosis.

Part 2 occupies itself with the chemistry of the urine.

Part 3 takes up the interpretation of blood chemical findings including such methods as sugar tolerance test, the blood sugar curve, its importance in encephalitis, in pregnancy and in diabetes. Some 25 pages are devoted to the subject of acidosis and nearly 100 pages to the question of nephritis.

Part 4 occupies itself with basal metabolism. This book will not only be found to be an adequate laboratory guide but will be of use to older practitioners particularly who have not kept up with every detail of modern advances and who may desire to brush up so as to understand the constantly increasing and changing chemical tests which are being used in modern clinical medicine. Many also will appreciate the footnote references to the literature. Everything is worked out with sufficient detail, including tables and charts so as to be of value to technicians in this field.

Marriott[21] delivered a series of six lectures to the San Diego Academy of Medicine in 1927, dealing with *Recent Advances in Chemistry in Relation to Medical Practice.* The first five lectures give an extremely good, clear, simple exposition of our present knowledge dealing with such fundamental facts as the atom, the molecule, the phenomena of dissociation, the hydrogen ion, surface tension and osmotic pressure. The topics of acidosis and alkalosis are then taken up; next the chemistry of the blood, foods and metabolism, vitamines and dietetics are discussed as well as a very simple milk mixture for infants. It would have been better if the final chapter on endocrines had been entirely omitted as this is superficial, fragmentary, and inaccurate.

Paul Lazarus edited the *Handbuch der gesammten Strahlenheilkunde, Biologie, Pathologie und Therapie.*[22] Two installments of vol. ii are on hand. This is the second edition of the *Handbuch der Radiumbiologie und Therapie.* The venerable Frederick Kraus writes the introduction

[19] **A Glasgow Manual of Obstetrics.** By S. J. Cameron, A. N. McLellan, R. A. Lennie and J. Hewitt. Edward Arnold & Co., London, 1924.

[20] **Blood and Urine Chemistry.** By R. B. H. Gradwohl and I. E. Gradwohl. C. V. Mosby Co., St. Louis, 1928.

[21] **Recent Advances in Chemistry in Relation to Medical Practice.** By W. McKim Marriott. C. V. Mosby Co., St. Louis, 1928.

[22] **Handbuch der gesammten Strahlenheilkunde, Biologie, Pathologie und Therapie.** Herausgegeben von Paul Lazarus. Zweiter Band. 1. Lieferung. 2. Lieferung. J. F. Bergmann, München, 1928.

just as he did in 1912 on the occasion of the appearance of the first edition. He regrets that the therapeutic results have not kept pace with the tremendous technical advances. He stresses the results obtained in rickets by means of natural and artificial light. The effect on leucemia by roentgen rays is praised. Lymphogranulomatosis responds most gratifyingly. The final results obtained with radiotherapy upon malignant tumors cannot yet be evaluated.

A number of well-known authors have been drawn upon for the revision. Holthusen discusses the biologic dosage to be used with the rays upon individual tissues, especially keeping in mind the radio sensitivity of normal and pathologic structures. The differences in result due to the quality of the rays must also be taken into account. Other effects are due to the size of the dose, as well as to its chronologic distribution.

Schwarz deals with the stimulation or "reiz" produced by roentgen therapy. He is unwilling to affirm or deny why the ray may exert a stimulus per se although stimulating effects may be obtained indirectly.

Rollier and Reyn speak of the method and technic of heliotherapy and chemical sources of light.

Wintz, whose work in gynecology is so well known, discusses the methods applicable to roentgen therapy. Hohlfelder deals with the fields to be applied while Werner discusses combinations with other therapeutic measures such as sensitization and desensitization. Groedel speaks of the injuries due to radiotherapy and the methods of avoiding them as well as of the legal consequences resulting from injury.

The second installment contains an article by Belot, the radiologist of l'Hôpital St. Louis, upon the roentgen and radium treatment of skin diseases including lupus, a very carefully arranged and well written contribution of nearly 100 pages.

The conclusion of skin diseases is dealt with by Degrais, including the treatment of angiomata, and by Pinch on the treatment of malignant skin lesions.

The subject of gynecology is taken up by three well-known contributors. To Seitz has been assigned the question of roentgen treatment in gynecology, including malignant neoplasms; x-ray castration, both temporary and permanent; so-called stimulating treatment to the ovaries; inflammatory gynecologic lesions, inclusive of tuberculosis of the tubes and peritoneum, and low dosage raying of the diseases of the external genitals. The author then enters into the details of the Seitz-Wintz method of treating malignant neoplasms, especially uterine carcinoma.

Von Seuffert discusses the treatment of malignant gynecologic lesions with radium in contradistinction with the preceding which dealt merely with the roentgen ray.

The concluding chapter is by Lahm who discusses the value of the malignancy index and such criteria as may be used in giving a prognosis based upon the histology of neoplasms.

Four installments of the *Handbuch der Inneren Sekretion*[23] have appeared since my last review.

[23] **Handbuch Der Inneren Sekretion.** Herausgegeben von Dr. Max Hirsch. 1. Band. Lieferung 4; II Band, Lieferung 4; III Band, Lieferung 5; III Band, Lieferung 6. Curt Kabitzsch, Leipzig, 1928.

Vol. i, installment 4, deals with two subjects. R. Jaffé and I. Tannenberg have written a long monograph on the adrenal. While most complete and thorough, their presentation lacks coordination and is therefore extremely difficult to read or review. The authors are inclined to ascribe the adrenal deficiencies noted in anencephaly to the same causes rather than to ascribe the cerebral malformation to lack of the adrenal cortex. They emphasize that the adrenal damage in infection runs parallel with the lipoid solubility of the poison and the cholesterol metabolism. The most recent American literature is not included in their review. In the same installment H. Josephy describes the normal and pathologic anatomy of the vegetative centers in the mesencephalon, in the sympathetic and parasympathetic systems.

Vol. ii, installment 4, contains an article on the physiology of the ovary by L. Adler who, it should be recalled, with Hitschman in 1911 overturned all the well established concepts concerning "endometritis" and introduced our modern conception of cyclic endometrial changes. The author discusses the subject in a very adequate fashion. He accepts my interpretation of the continuation of the action of the follicle by the corpus luteum.

Rosenberg in the same installment deals with the normal and pathologic physiology of the internal pancreas secretion.

Of the third volume, the fifth installment contains an article by Leicher on the internal secretion and diseases of the ear, upper respiratory and intestinal tracts. As far as the ear is concerned, endemic cretinism, acromegaly, otosclerosis, especially in connection with the genital phases, is taken up, a special chapter being devoted to the ear and the sex organs. The same diseases are discussed in connection with the nose and sinuses. The relation between the hypophysis and nasal diseases is dealt with, transnasal operation for pituitary tumor being pictured in detail.

The same author discusses the influence on the larynx, trachea, and bronchi on abnormalities of the thyroid and thymus glands, as well as the laryngospasm in asthma as affected by endocrine disturbances.

H. Hirschfeld has dealt with the subject of internal secretion and blood diseases.

Bingold and Delbanco have written on the internal secretions and skin.

Vol. iii, installment 6, contains the article by Pulvermacher, "Is the Skin an Organ of Internal Secretion?" He answers this question in a rather ambiguous fashion, considering the skin an organ of internal secretion only if we enlarge that concept to include all cells, tissues and organs which influence other structures through humoral channels.

In this installment M. Rosenberg has another extensive article on the pathology of the internal secretion of the pancreas.

Von Szily and Poos describe the effect of the internal secretion on the eyes while the installment is concluded by an article by Kranz on the internal secretions and dentistry. The series is proving to be of great importance, a high standard of excellence being maintained throughout. I have given up the hope of finding a return to the pre-war Handbuch with its carefully worked up and really complete bibliography. Times have changed; production has increased at such a rate as to nullify a world-wide bibliographic reference except in an index medicus.

Laquer has written a short résumé of our present knowledge of hormones and internal secretion[24] which on the whole, in spite of its brevity, is informing. Naturally in the present state of knowledge, no single individual is fully conversant with every aspect of internal secretion. Consequently the different chapters are somewhat uneven. This short treatise is one of the best written.

The second edition of Cumberbatch's *Diathermy*[25] has appeared after an interval of six years and because of the many advances, especially in the design of the diathermy apparatus, has been considerably increased in size. The first half of the treatise is devoted to a full description of high frequency currents, their method of production, the machines employed, distribution of currents, and the resultant heat production in the tissues.

In gynecology, Cumberbatch and his coworkers at St. Bartholomew's Hospital have found that heat production cures urethral and cervical gonorrhea in the course of 3 to 5 applications. Gonococci are no longer found in the tissues, recurrences do not take place and several patients have married without infecting their husbands. In addition to cervical and urethral treatment, heat is applied to the ovaries, tubes and parametrium with a consequent relief of pain and disappearance of exudates. Reports on the other diseases affected favorably by diathermy, such as dysmenorrhea, menorrhagia, etc., are less convincing. The author discusses the use of diathermy in all sorts of diseases such as peripheral neuritis, trigeminal neuralgia, arteriosclerosis with high blood pressure, hemorrhoids, colitis, pneumonia, to quote only a few.

The final chapter contains a description of high frequency currents in surgery. This includes different technics such as fulguration, actual cutting with the diathermy knife, electrodesiccation, etc. This book is a sensible, dignified discussion of this important field of medicine in which the enthusiasm of a pioneer is kept well within the bounds of sound reason and discretion.

The fourth edition of Hertzler's *The Technic of Local Anesthesia*[26] has just appeared. The author emphasizes the fact that each case presents an individual problem. I still cannot acquiesce in his counsel not to boil the novocaine tablets at all but simply to drop the tablets into sterile water. The great majority of surgeons will agree with Hertzler in frowning on the use of splanchnic anesthesia.

The book first gives general technics of anesthesia and then deals with special locations throughout the body. This popular monograph is a good general guide. The addition of some good anatomic charts would add to the value of the volume.

Levinson has published a second edition of *Examination of Children by Clinical and Laboratory Methods.*[27] This short, concise, well-arranged book deals entirely with methods of examination as well as their interpretation. The new edition keeps well up to the changes which have occurred in the last few years.

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[24]**Hormone und Innere Sekretion.** Von Dr. Fritz Laquer. Theodor Steinkopff, Dresden und Leipzig, 1928.

[25]**Diathermy.** By E. P. Cumberbatch. Ed. 2. C. V. Mosby Co., St. Louis, 1928.

[26]**The Technic of Local Anesthesia.** By Arthur E. Hertzler. Ed. 4. C. V. Mosby Co., St. Louis, 1928.

[27]**Examination of Children by Clinical and Laboratory Methods.** By A. Levinson. Ed. 2. C. V. Mosby Co., St. Louis, 1927.

The tenth series of *Methods and Problems of Medical Education* published by the Rockefeller Foundation in 1928[28] is really a world's tour through the physiologic, pharmacologic, bacteriologic and pathologic laboratories of this world. Any one desiring to find the data for planning such medical workshops will do well to consult its pages.

Vol. ii and vol. iii of the 38th Series of *International Clinics* (June and September, 1928)[29] are on hand. Of the huge variety of material dealt with, few lend themselves for review. Bleeding from the nonpregnant uterus; chronic salpingitis; chronic appendicitis by J. B. Deaver contain nothing new. Sajous in a long article, "Rational Endocrinology and Organotherapy as Foundations for Greater Efficiency in Practice," asserts that the adrenals are dominant agents in pulmonary and tissue respiration. Adrenal secretion according to the author converts the hemoglobin into oxyhemoglobin. He even assigns a definite function to the thymus. In contradistinction to this entirely unwarranted assumption, he denies all real endocrine action to the pituitary thereby ignoring all recent well substantiated work.

William P. Smith, in operating upon prolapse of the uterus, favors the interposition operation.

Cancer and Cancer Research[30] is a brochure intended for the lay public and compiled from articles which appeared in the Liverpool *Daily Post and Mercury*. The Committee bolsters up its claims with a somewhat weak endorsement taken from writings by Drs. Francis Carter Wood, Bloodgood, and Graves. The whole theory is apparently based on the fact that lead is toxic to embryonal cells. The entire brochure is well written and replete with general information but on the whole must be regarded as propaganda for the Liverpool lead treatment.

Selected Abstracts

Obstetric Operations

Gibberd, G. F.: Induction of Labor With Animal Bladders Containing Glycerine. Lancet **1**: 1325, 1928.

It is suggested that a pig's bladder, capacity of 500 c.c., or a sheep's bladder, capacity of 150 c.c., containing glycerine, supplement the bougie or bag frequently used in inducing labor. The bladders are sterilized and packed in alcohol. The bags are inserted just through the internal cervical os, and then about one-fourth filled with glycerine. As this substance is hygroscopic, the size of the bladder is gradually increased by osmosis.

The possible dangers are infection and harmful effects of glycerine. The glycerine might, with its irritation, produce shock, or increase the uterine contractions, or if enough was absorbed, produce a nephritis.

No positive conclusions are made, and no advantages of this method over similar procedures are indicated. H. C. HESSELTINE.

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[28] **Methods and Problems of Medical Education (10th Series).** Division of Medical Education. The Rockefeller Foundation, New York, 1928.

[29] **International Clinics.** Vols. ii and iii, 38th Series. J. B. Lippincott Co., Philadelphia, 1928.

[30] **Cancer and Cancer Research.** Compiled by a Scientific Committee of the Liverpool Medical Research Organization. Sherratt & Hughes, Manchester, 1928.

De Guchteneere: Medical Induction of Labor. Bruxelles-med. 8: 1208, 1928.

Medical induction of labor was attempted in 24 cases. In 15 instances the membranes were intact and of these 12 (80 per cent) responded to treatment. In the remaining 9 cases the membranes were ruptured and all of them responded to treatment. Thus the medical induction was successful in a total of 21 (87.5 per cent) cases.

The technic used in this series consisted in the administration of 4 doses of quinine (sulphate or chlorhydrate) of 0.5 gram, each at half-hour intervals and up to 8 subcutaneous injections of ¼ c.c. of pituitrin at half-hour intervals, the first injection being given one-half hour after the fourth dose of quinine. If labor did not begin following the injection of pituitrin, the entire procedure was repeated twenty-four hours later.

In 4 cases it was necessary to repeat the routine once and in one case twice. There were 3 failures. One labor started spontaneously forty-eight hours after the treatment; a second patient was probably not at term, and the third showed vagotonic symptoms.

Quinine and pituitrin strengthen sufficiently the physiologic contractions of the uterus to force the presenting part against the cervix and cause beginning of dilatation. The presenting part then acts as a mechanical stimulus and labor continues spontaneously. For this reason Guchteneere believes that, if the cases where the membranes have ruptured be excluded, only about 80 per cent success may be expected from this method.

He concludes that medical induction of labor is an extremely useful procedure in many cases such as postmaturity, disproportion and toxemias of pregnancy. If it is carefully carried out it is a safe method but accidents may occur.

THEODORE W. ADAMS.

Delmas, P.: Extemporaneous Evacuation of the Uterus at the End of Pregnancy. Bull. Soc. d'obst. et de gynée. 17: 413, 1928.

The author advocates forcible dilatation of the cervix at the end of pregnancy in selected cases. He administers spinal anesthesia, manually dilates the cervix, and performs a version and extraction or if the latter is not feasible, he delivers the baby with forceps. After delivery he injects iodine into the uterine cavity, and if the membranes have been ruptured a long time, he inserts into the uterus a tampon saturated with bouillon vaccine. In addition he gives a prophylactic subcutaneous injection of sulpharsensol.

Of the 40 cases reported, in the author's opinion not one mother died or was injured as a result of the operation, since the one maternal death he attributes not to the procedure but to placenta previa. All the babies which were alive before extraction were born alive.

The entire operation lasts only about fifteen minutes. The dilatation of the cervix consumed from twenty seconds to twelve minutes but the usual duration was three minutes. The delivery of the child never required more than six minutes. The delivery of the placenta usually required from three to six minutes.

Among the indications for the operation are eclampsia, premature rupture of the membranes, placenta previa, and fetal asphyxia. The procedure is advocated for specialists only because in the hands of the inexperienced, harm may result.

J. P. GREENHILL.

Houël and Jahier: Prophylactic Fixation of the Anterior Arm in Performing Version and Extraction in Head Presentations. Bull Soc. d'obst. et de gynéc. 14: 214, 1925.

Prophylactic fixation of an arm is an accepted procedure in cases of transverse presentation but no one has ever before advocated this procedure in cases of head presentation. The authors fixed the anterior arm with a sling in all cases of head presentation where version and extraction were to be performed. There was neither mortality nor morbidity for the mothers. Two of the children died twenty hours after birth, one from eclampsia and the other was a blue baby. In all the cases delivery was easily accomplished.

The anterior arm should be fixed in preference to the posterior because an anterior asynclitism, which is more favorable than a posterior asynclitism, is produced. There is then less danger to the perineum.

J. P. GREENHILL.

McGuinness, F. G.: Prophylactic External Version in Breech Presentation. Canad. M. A. J. 18: 289, 1928.

The author strongly favors prophylactic external version as a routine in uncomplicated breech presentations to avoid an increased fetal mortality. He does not mention any contraindications to this type of version. According to his report, the dangers of infection and extensive perineal laceration are greater in breech delivery, both in primiparae and multiparae.

He discredits the danger of partial separation of the placenta as well as the possibility of inducing premature labor. The number of cord complications was not increased. Those cases that revert have a repeated external version. Binders were used when necessary.

H. C. HESSELTINE.

Fruhinsholz, A.: A Case of Fetal Death Following External Version. Bull. Soc. d'obst. et de gynéc. 26: 409, 1927.

In a twenty-two year old primipara a breech presentation was found in the beginning of the eighth month of pregnancy. Three attempts on different occasions to perform an external version were unsuccessful. Hence, an attempt was made under anesthesia with the patient in the Trendelenburg position. This was successfully accomplished with ease but the fetal heart tones became slower and irregular. In the belief that this was due to fetal discomfort, an abdominal binder was applied. About ten minutes later bleeding began and continued for part of a day. A few hours later painful contractions started and the fetal heart tones disappeared. The uterus became permanently firm and at the end of forty-eight hours, a macerated fetus was spontaneously expelled. The placenta was small and the cord was inserted marginally. There were no blood clots on the uterine surface of the placenta. Fruhinsholz believes the cause of fetal death in this case was direct pressure of the fetal head on the vascular branches at the insertion of the cord into the placenta. For placental separation to account for the death, there would have had to be an extensive separation and there was no anatomic evidence of this.

The accident which occurred in this case is rare and should not be held against the performance of external version. The author has, in some cases of external version, seen mild bleeding, transient fetal distress or uterine hardening without any serious consequences.

J. P. GREENHILL.

Araya: A Method of Accomplishing Internal Podalic Version in the Absence of Amniotic Fluid. Semana méd. 31: 349, 1924.

Araya describes a modified Champetier de Ribes bag used by him since 1905, consisting of an elastic bag of the conventional form penetrated by a rubber tube which emerges through the center of its base. Through this tube normal saline solution is injected into the cavity of the uterus after the bag has been introduced and filled in the ordinary way. This form of bag has been found most useful in cases in which podalic version was questionable either because of insufficient dilatation, lack of amniotic fluid, or both. The author prefers to administer chloral or laudanum by rectum as a preliminary measure, or, in cases of tetanization of the uterus or of Bandl's ring, to anesthetize the patient with chloroform. With the patient in Trendelenburg position the bag is inserted and distended, and then saline solution up to 300 or 500 gm. is run through the tube into the uterine cavity, always in the intervals between contractions. As the bag finally is expelled through the cervix, the hand is promptly introduced into the vagina, and passed into the uterus. With the injected fluid still in utero the version is greatly facilitated. Eight cases are reported in detail where this form of bag has been used. The author believes that it would be of value as a hydraulic method of restoring an inverted uterus.

THOS. R. GOETHALS.

Fernandez: Maneuver to Overcome the Difficulty Caused by Bandl's Ring in Internal Podalic Version. Semana méd. 33: 1241, 1925.

Fernandez finds that when version is rendered difficult or impossible of accomplishment due to contraction or retraction of the uterus such contraction is seldom in the form of a clearly defined ring. More frequently there is a more or less generalized contracted state which is, however, most marked at certain regions, e.g., the occipitodorsal region in occipital and face presentations, and at the angle formed either by head and shoulder or between head and trunk in the transverse presentations. Such "rings" or areas of most marked contraction are apt to be torn through in any classical method of version and to result in extensive tears or rupture of the uterus.

The author suggests that after both feet have been brought down if possible, or one foot in any case, the baby's body should be rotated by combined pressure from above and rotation of the fetal pelvis by means of the feet or foot in such a way as to swing the occiput away from the area of greatest contraction into the opposite iliac fossa. Thus, the way is cleared for the head to rise up in the uterus while the fetal pelvis dilates the contraction in its descent.

Seven cases have been successfully delivered in this way by the author and three colleagues.

THOS. R. GOETHALS.

Fischer, G.: Some Observations on Craniotomy at the Woman's Clinic at Lund. Acta obst. et gynec. Scandinav. 6: 144, 1927.

During the years 1900 to 1925 there were 42 craniotomies performed at the Lund clinic and three of these on living children. The incidence of craniotomies was 0.18 per cent. In 32 per cent of the cases a contracted pelvis was present. Five of these patients subsequently became pregnant but only one had a normal delivery. Among the 42 patients, 71 per cent were primiparae and the majority of them were over thirty years of age. There occurred not a single maternal death in the entire series but in 57 per cent of the cases there was fever after delivery. In half of these cases, however, fever had been present before the craniotomy.

J. P. GREENHILL.

Stoeckel, W.: Unsuccessful Obstetric Attempts. Monatschr. f. Geburtsh. u. Gynäk. 75: 7, 1926.

The author reviews 55 cases where operative procedures were unsuccessfully instituted in the patients' homes, in an attempt to effect delivery. These patients were then sent to a hospital. The cases are divided into two groups; namely, (1) those in which there were proper indications and correct attempts, and (2) those in which there were false indications and incorrect attempts which necessarily resulted in failure.

In the first group there were a number of operations attempted in the presence of fetal death, and other cases in which fear of destructive operations, such as, craniotomy and decapitation, prompted unnecessary haste with consequent maternal injury.

The second group comprises 39 of the 55 cases and in all of them high forceps operations were attempted which from the outset were doomed to be unsuccessful. In only 2 of these cases were the conditions for a forceps delivery fulfilled. The same was true of the indications for the operations.

Only in 24 of the 55 cases was information obtained concerning the indication for the attempted operation. Even where information was given it was often of such a character as to hide the truth and to mislead the hospital authorities, so that cesarean sections were done where proper information would have revealed the risk of such operations.

Of the 55 children, 25 were born alive and 2 of the latter died shortly after birth from trauma. Four of the mothers died and 20 had a long febrile puerperium.

The chief cause for these mistakes is not lack of skill and experience but false obstetric thinking, the lack of appreciation of the significance of conditions and indications, and of ignorance of the fact that occasionally the life of a child must be sacrificed in the interest of the mother. The teaching that labor should not be hastened must be emphasized again. The author agrees with those who advocate the delivery of a baby with forceps after the head has remained at the outlet for a long time. But all are agreed on the seriousness of high forceps operations. The author values the Kielland forceps highly but believes that they should be used only by an experienced individual.

Another cause for the bad results in obstetrics is inadequate teaching in the medical schools.

J. P. GREENHILL.

Miller, Douglas: The Failed Forceps Case and its Treatment. Brit. M. J. 2: 685, 1927.

In a series of 500 emergency admissions to the Edinburgh Royal Maternity Hospital, it was found that in 88, or 17.6 per cent, forceps had been applied and efforts made at extraction without the desired result.

The commonest individual cause of failure was disproportion, being found in about 40 per cent of cases. A posterior position of the occiput was found to be an almost equally common cause of difficulty. A third group comprises cases in which no abnormality of the pelvis was present, the child was of average size, presentation and position were normal. Finally, there were two face cases, one of them a mentoposterior, one brow presentation, and one case of ovarian tumor obstructing labor.

Approximately one-third of these patients were seen by a physician for the first time after the commencement of labor. There were only three failed forceps cases among more than 6,000 patients who attended the hospital antenatal clinic.

Where moderate forceps traction fails to effect delivery, the following question must be answered: (1) What is the nature of the obstruction? (2) Is birth of a living child *per vias naturales* possible? (3) If delivery by the natural passages is contemplated, is immediate intervention in the interest of mother or child desirable or not? (4) If delivery of a living child through the vagina is impossible, do the conditions present warrant or forbid cesarean section?

Seventeen of the 88 patients died, a mortality of 19 per cent. The individual causes of death were: sepsis 12, rupture of the uterus 2, postpartum hemorrhage and shock 2, and eclampsia 1. In addition, in 39 (44.3 per cent) the puerperium was morbid. Few patients escaped without more or less serious laceration of cervix, vagina or pelvic floor. Including stillbirths and neonatal deaths, 46 of the infants were lost, a mortality of 52 per cent.

ADAIR.

Hendry, James: Unsuccessful Forceps Cases (How far can they be prevented by efficient antenatal care?) Brit. M. J. 2: 135. 1928.

In estimating how far the cases of "failed forceps" could have been prevented by efficient antenatal care, Hendry shows that almost all of the real abnormalities could have been identified during the course of pregnancy, and particularly in the last month. There is only a very small group of fetal abnormalities of the developmental type which cannot be detected before the onset of labor. Antenatal supervision, however, cannot prevent the too early application of forceps in normal cases.

When abnormalities have been detected they may either be corrected before the onset of labor, as in occipito-posterior, breech, and transverse presentations, or patient sent to a hospital where appropriate treatment can be carried out under the most favorable circumstances at the correct stage in labor.

The antenatal supervision can be efficiently carried out by the family physician in many cases, but there always remains a considerable proportion of cases in which accurate diagnosis of pelvic disproportion or abnormal presentation is difficult. An efficient obstetric service would require well-equipped consultative antenatal centers to which the cases presenting difficulites to the family physician can be referred. Hendry believes that a midwife should not be authorized to undertake the care of any pregnant woman without provision being made for the patient to be examined carefully by a medical practitioner before labor is due.

PROSHEK.

Miller, Douglas: Observations on Unsuccessful Forceps Cases (Causation, Management, and End Results). Brit. M. J. 2: 183, 1928.

The unsuccessful forceps case would appear to be largely the outcome of nonobservance of one of three elementary rules in regard to forceps operation. First, that forceps should not be applied in the presence of marked disparity in relation to the head and pelvis, and rarely, if ever, when the head is still movable above the pelvic brim. The frequency with which it was found that forceps delivery had been attempted while the head was still unengaged would indicate that the difficulty and danger of the high forceps operation are not sufficiently appreciated. Secondly, that forceps should not be applied without an exact knowledge of the position which the head occupies in the pelvis. The initial mistake in unsuccessful forceps cases is so frequently one of diagnosis that it would appear necessary to re-emphasize the wisdom of the time-honored dictum "chloroform and the whole hand" as a preliminary to forceps application. The third essential is that the cervix should be completely effaced and retracted over the presenting part.

PROSHEK.

Shaw, William Fletcher: Unsuccessful Forceps Cases. Brit. M. J. 2: 188, 1928.

In teaching clinical obstetrics special emphasis must be laid upon certain sections of the work, and if this is done the graduate of the future will be turned out capable of taking charge of normal cases, of recognizing abnormalities, and of treating the minor ones, and with a sound clinical foundation upon which to build with future experience. The following four topics are of importance and require special emphasis: antenatal work; antisepsis; first stage of labor; and importance of making a definite diagnosis before applying high forceps.

PROSHEK.

Schockaert: On the Application of Forceps in the Superior Strait. Bruxelles-méd. 8: 708, 1928.

Undoubtedly the scope of cesarean section has been widely increased with the improvement of asepsis and technic. The low cesarean has even increased this field so that the operation can be applied in even potentially infected cases. However, there are cases of moderate disproportion when the woman has been in labor a long time, the membranes have been ruptured for many hours and the amniotic fluid infected, when one hesitates to do even an extraperitoneal cesarean. It is in these cases, where the fetus is still living, that in Schockaert's opinion the use of high forceps should not be entirely disregarded.

THEODORE W. ADAMS.

Franqué, O: Evil Results of High Forceps Operations (Rupture of the Uterus, Air Embolism, Separation of the Pelvis, Lacerations of the Bladder) and Their Prevention. Med. Klin. 24: 401, 1928.

The author relates a series of cases in which extensive damage followed the application of high forceps. The first case was one of rupture of the vagina and uterus, and the patient died of peritonitis. The author believes the forceps operation was unnecessary and the patient's life could have been saved if she had been taken to a hospital before the forceps were applied. The operation was performed because of irregularity of heart tones due to the use of pituitary extract. The second case was one of air embolism after extensive injury to the cervix, and this patient also died. The third case was one of rupture of the symphysis during a high forceps operation. In the fourth case, there was not only a rupture of the symphysis but also a laceration of the bladder. This patient had a cephalo-pelvic disproportion and a cesarean section should have been performed.

The author emphasizes that high forceps should be used only when there is serious danger to mother or child and a version and extraction cannot be performed. There must be no disproportion between the fetal head and the pelvis and the head must not be floating above the inlet. In the home, if the operation does not progress favorably, one dare not resort to excessive force but must perform a craniotomy. The latter operation is indicated if the head does not descend after ten to twelve powerful contractions. The obstetrician should use one type of forceps for all his operations and not burden himself with a new type of instrument every few years.

J. P. GREENHILL.

Varo, B.: Forceps Applied to the Breech. Monatschr. f. Geburtsh. u. Gynäk. 73: 46, 1926.

The author reports that in his clinic the Kielland forceps were employed to deliver 7 cases of breech presentation. The forceps hold the breech best when

they are applied to the hips, and thus grasp bony prominences, the iliac crests and the greater trochanters of the femurs. When the back of the child is to one side of the mother, such a grasp is impossible with the usual type of forceps, because they cannot be applied in the antero-posterior diameter of the pelvis. Therefore, the Kielland forceps should be used for breech presentations. Proper application of these forceps to the breech is not more dangerous to mother and child than the application of forceps to the head.

J. P. GREENHILL.

Küstner, O.: The Operative Treatment of Breech Presentation. Monatschr. f. Geburtsh. u. Gynäk. **78**: 379, 1928.

The application of the usual cephalic forceps has been advocated for the delivery of a breech by a number of authors. Küstner, however, feels that these forceps should not be used because they do not fit the breech and, therefore, cause damage. He advocates a specially constructed wide, blunt hook which is applied to the posterior hip. The hook was used in 40 cases and over a period of years was used in from 0.8 to 5.6 per cent of all the breech cases. No mother was lost and all but two of the children who were alive before the hook was applied were born alive. The two exceptions required craniotomy on the aftercoming head. Maternal injuries consisted of 2 third degree lacerations in elderly primiparae and a vesico-vaginal fistula. Fetal damage consisted in two fractures of the neck of the femur and a few skin lesions. The author believes the use of this hook should be taught to students to the exclusion of all other methods.

J. P. GREENHILL.

Zarate, Enrique: Partial Symphysiotomy and the Symphysiotomy of Frank. Gynéc. et Obst. **14**: 289, 1926.

The author feels that the technic of Frank is complicated and dangerous and that it nearly always entails section of the corpus cavernosum and the ligament of Henle and endangers the clitoris and urethra. The technic outlined by the author differs in the fact that, by an oblique insertion of the knife exactly at the upper border of the fibro-cartilage of the symphysis, the operator actually sections only the fibro-cartilage between the bone surfaces, leaving most of the anterior ligament, all of the posterior ligament and the ligament of Henle, which serve as restraints, when the joint surfaces are separated by distinctly forceful abduction of the thighs. There is a minimum of danger in this procedure and the technic is simplified so that the operation is safe under almost any circumstances. The separation of 5 cm. at the symphysis which the operation allows, will permit the passage of the fetal head in all pelvic contractions down to an obstetric conjugate of 8 cm.

The author believes that this operation should absolutely eliminate the use of high forceps and restrict the number of cesarean sections for pelvic contraction. It can be done so rapidly and simply as to be of value in delivering the aftercoming head, and is easily accomplished in the home.

GOODRICH C. SCHAUFFLER.

Fossati: Permanent Enlargement of the Pelvis. Annali di Ostetricia e Ginecologia **46**: 611, 1924.

Seven cases of partial symphysiectomy are reported in this article. All were primigravidae with flat rhachitic pelves, true conjugates varying from 7.8 to 8.2 cm. Operation was done during labor in 4 cases; twenty days antepartum in

one; and as addition to abdominal cesarean in two. Babies weighed from 2900 to 3720 gm. Of the five delivered through the vagina following the operation, one baby was expelled spontaneously, stillborn; on one craniotomy was done because of disappearance of fetal heart tones and rigidity of maternal tissues; two babies could not be resuscitated following forceps delivery; one born by version was living and healthy. The two born by cesarean were in good condition.

The first case of the series suffered a diastasis of symphysis without injury to bladder as result of difficult forceps delivery. The fourth case caused trouble during operation by bleeding extensively from prevesical venous plexus; although her baby was delivered stillborn, spontaneously, five hours after operation she gave birth spontaneously 3 years later to a healthy baby weighing 3320 gm.

Operations for permanent enlargement of the pelvis comprise two types, partial symphysiectomy (Costa), and resection of the promontory (Rotter-Schmid). The two operations may be combined in the same case. Author believes that with a true conjugate of 8 cm. partial symphysiectomy is the operation of choice save in those cases where an acute projection of the promontory is the sole cause of the shortening; where the conjugate is between 7 and 8 cm. the two operations are best combined in order to avoid removal of too much of the promontory. These operations properly used offer the advantage of bringing about a permanent enlargement of the pelvis and they should be performed in connection with the cesarean section.

THOS. R. GOETHALS.

Schmidt, W. Th.: A Successful Case of Hebosteotomy with an Auto-Transplantation Between the Severed Ends of the Pubic Bone. Monatschr. f. Geburtsh. u. Gynäk. **68**: 96, 1925.

A left-sided hebosteotomy was performed on a twenty-six year old primipara. The cut ends of the pubic bones were kept about 6 cm. apart with a special dilator and the child was extracted with forceps. Then about 3.5 cm. of the upper part of the left pubic bone was removed and the excised piece of bone placed between the ends of the pubic bone at the hebosteotomy incision. The muscle attachments previously freed were sewed to the transplant and the wound closed. The patient had a stormy convalescence for a week, and fistulae developed in the wound. Despite this, the patient was permitted to walk. The fistulae closed but one reopened again several weeks later and pieces of bone were removed from it. At the site of the transplantation there was a strong bony bridge. The patient subsequently became pregnant and after a three-hour labor, spontaneously delivered a baby which weighed 8 pounds. The first baby had weighed 6¾ pounds.

J. P. GREENHILL.

Odagesco, S.: The Results of Expectant Treatment in Contracted Pelves and the Test of Labor. Rev. franç. de gynéc. et o'bst. **19**: 493, 1926.

In the author's clinic it was found that when women with contracted pelves were given a test of labor, 70 per cent delivered spontaneously. In the remaining 30 per cent no bad results were noted because of the test of labor and this was due to the fact that in many of these cases the low, cervical cesarean section was performed. This type of cesarean section is the operation of choice even in unclean cases.

From 1921 to 1926 at the Tarnier clinic, 70 women with contracted pelves delivered spontaneously. In 8 cases a pubiotomy was done and in 4 cases a symphysiotomy. In 5 of these 12 cases serious complications occurred. Eighteen cesarean sections were performed of which 5 were classic and 13 low, cer-

vical. Among the latter cases labor had lasted from twelve to forty-eight hours and the membranes had been ruptured from three to twenty-two hours.

All the patients recovered and all the babies were alive. A comparison of pubiotomy, the classic cesarean section, and the low, cervical operation clearly showed the superiority of the last named.

J. P. GREENHILL.

Titus: Episiotomy and the Immediate Postpartum Repair of Both Old and New Perineal Injuries. Am. J. Surg. 3: 499, 1927.

Titus advocates episiotomy preferring the median incision to the lateral. He claims for it less injury to the muscle and better approximation. A number of excellent drawings illustrate the technic. Immediate repair is made of any laceration of the perineum. In multiparae with posterior vaginal and perineal relaxation a gynoplastic repair is made at time of subsequent delivery, especially if there is an abrasion of the mucous membrane.

More extensive gynoplastic work on the cervix or the bladder floor for chronic lesions is a dubious procedure at the time of delivery. Likewise, such operations during the early puerperium offer little advantage over a secondary repair at a later date after involution is complete.

WILLIAM KERWIN.

Bucura, C.: The Constitutional Indications For Episiotomy. Wien. klin.Wchnschr. 37: 387, 1924.

The author agrees with v. Jaschke that prolapse following childbirth cannot be explained on a mechanical or traumatic basis alone, and believes that every case presenting such pathology has, as an underlying factor, an inferior development with weak and underdeveloped tissues. As proof of this theory, he cites the many cases of prolapsus uteri found in nulliparae and even in virgins. There are two factors concerned in the development of prolapsus: (1) the trauma, and (2) which is the more important, the inherent failure of the supporting tissues to fully develop. The latter cannot be corrected. and massage and gymnastics will not induce full development. Prolapse, however, is prevented to a great extent if the factor of trauma can be eliminated by preventing any overstretching of the birth canal. This can be done by a deep incision extending as high as possible up the birth canal. "Episiotomy should, therefore, be performed in all cases of infantile, asthenic and inferior genitalia not as taught in the textbooks when rupture of the perineum is imminent, but at the time when overstretching is first threatened." The author believes that such a routine procedure would prevent many cases of prolapsus. When performed correctly there is no trauma to the tissues and a careful anatomic repair will restore the parts to their original construction. The author has used this method for fifteen years and states that he has seen no failures, either primary or secondary, even though many cases have gone through repeated labors. He stresses the importance of the exact indication and of the time of performing episiotomy.

RALPH A. REIS.

Correspondence

Routine Removal of the Appendix in All Abdominal Operations by a Suitable Technic.

To the Editor: Twenty-five years ago in an article contributed to the Cincinnati *Lancet-Clinic* I was the first, I believe to urge the routine removal of the appendix when it could be readily reached during an abdominal operation. I had previously made a careful study of the appendix in 636 cases in which it had been thus removed. Of those 636 cases the appendix was found thickened in 126; adherent to the intestines in 90; to the gall bladder in 4; to the omentum in 3; to the ovary in 30; to the fallopian tube in 36; partly obliterated in 65; club-shaped in 63; constricted in 22; thickened and swollen in 116; containing fecal concretions in 13 (3 concretions in one case, 5 in another and a seed in a third); cystic in 2; twisted upon itself in 23; atrophied throughout in 16; *apparently* normal in 27. During the period covered by those 636 cases, I operated on seven cases of acute appendicitis in which the abdomen had been previously opened but the appendix ignored and since then have removed a large number of appendices thus left behind.

Shortly after the publication of that paper Dr. Howard Kelly published an article in which he disapproved of such routine removal; but I note with satisfaction that in the preface to the last edition of his *Gynecology*, just published, in mentioning the improvements which have come into our work during the intervening years, he speaks approvingly of "extirpation of the appendix" in connection with other abdominal operations.

After many years of apparent acquiescence in this view, and the evident wide-spread adoption by surgeons of the idea of such removal, it came as a great surprise and distinct shock that Dr. J. O. Polak, in his "Study of Mortalities" (Am. J. Obst. and Gynec., 16, 600, 1928), should state that such "routine removal adds to the morbidity and often to the mortality." The feeling of surprise was not lessened when Dr. Baer of Chicago voiced his approval of the view in the discussion which followed the reading of the paper.

Correspondence with these surgeons has shown, as suspected, that the technic used in the removal of the appendix might readily account for the alleged morbidity and "often" mortality.

During the twenty-five years since my article appeared in the *Lancet-Clinic*, I have done such routine removal of the appendix not less than 10,000 times, and my associates have so removed it in many other thousands of cases. In my own work I have not had a single instance in which I could attribute any morbidity and certainly no mortality to such removal, and my associates assure me that with them has there been no positive suggestion of any increased morbidity and no mortality. The method of removing the appendix which I have used is so simple and prolongs the operation by such a negligibly short time that I cannot conceive of its being responsible for any form of subsequent trouble. Of course in desperate cases in which the loss of even a few moments might jeopardize the life, no surgeon would pay any attention to the appendix unless he had positive reason to believe that it was an integral part of the trouble for which he was operating.

In all suitable cases of gall bladder surgery and of right inguinal hernia, I remove the appendix if within reach. If the appendix is high up I do not enlarge the hernial opening for the purpose of removing it unless there is a history that it has been a source of some trouble.

The technic used in my thousands of cases is as follows: (1) The appendix and adjacent portion of the cecum are brought into view, and the cecum is so held by

the fingers of an assistant with a piece of gauze. (2) With a hemostat the mesoappendix is transfixed at its base, a catgut ligature withdrawn, and the mesoappendix ligated at its base and severed just beyond the ligature. (A second or third ligature is used if the mesoappendix is unusually broad.) (3) With a chromic catgut ligature the appendix is tightly tied close to the bowel, the ligature held taut with the thumb and forefinger, a hemostat applied just beyond the ligature to retain the contents of the appendix and the appendix severed with scissors so as to leave a safe "button." (4) With a small probe dipped in pure carbolic acid the mucous membrane and the edges of this button are thoroughly sterilized. The surplus acid is wiped away, and frequently the mucous membrane comes away with the wipe as it has been separated by the tight ligature. Particular care should be taken that the carbolic acid is worked down to the very bottom of the projecting button. The ligature is then cut short and the cecum dropped.

By the above technic it will be noted that at no time does the interior of the appendix come in contact in any way with the incision, nor is the cecum released until after most effective sterilization of the inside of the button, so that infection has been absolutely excluded from start to finish. Furthermore, there is no devitalized tissue, the result of the use of the actual cautery or crushing clamps, left behind for nature to care for. The prudent operator will, of course, in the rare cases in which an unusual amount of raw surface is exposed, whip the peritoneum over for protection, but such is entirely unnecessary for the small surface usually left. (A good many years ago, following the dictum of the late Seneca D. Powell, I thought it necessary to "neutralize" the carbolic acid by alcohol, but on the appearance of the article by Clark and Brown in the *J. A. M. A.* of March 17, 1906, in which it was demonstrated that alcohol was in no sense a neutralizer, I abandoned this step of the operation as a waste of time and alcohol.)

I have reopened the abdomen for one purpose or another in a considerable number of cases in which such routine removal of the appendix had been previously practiced, and in not a single instance was there the slightest evidence that such removal had been a source of any trouble whatever.

The operative technic, which I think has been responsible for all the morbidity and mortality attributed to the routine removal, constitutes in itself a more or less complicated operation. Usually by this technic the appendix is ligated and cut away, and the stump is treated by the actual cautery or by carbolic acid and alcohol; then the operator passes a purse string around the stump about one-half inch distant, pushes the stump down and then ties the suture. He has thus buried the stump in a moist and warm crypt *which constitutes an ideal incubator for the rapid production of microbes.* At the same time his suture has necessarily cut off a part of the blood supply to the piece of cecal wall which it encircles. The needle wounds which he has made through the peritoneum and muscularis afford a number of minute points for the possible escape of bacteria with resulting infection, and perhaps even the mucous membrane itself may have been penetrated by the needle or by the suture following. Furthermore, the operation consumes a very appreciable length of time. (Inversion of the open stump of the appendix with closure with purse string [Dawbarn's method] obviates the menace of the incubation chamber but does not prevent the possible escape during the manipulation of some intestinal contents; while several deaths from hemorrhage have been reported.)

Surgeons who use the above method should certainly read those illustrated pages in *Operative Surgery* in which J. Shelton Horsley shows the imminent danger of this procedure. They should also read the equally vigorous condemnation of this method by Franklin I. Harris of San Francisco, published in *California and West Med.* 27, 69, 1927. It does not seem possible that any surgeon would consent to employ such an elaborate and dangerous technic after reading these two articles when a different procedure with its beautiful simplicity and rapidity seems to meet all the

objections that can be urged against the other. Certainly in a suit for malpractice resulting from the unfortunate termination of such technic, the defendant would have considerable difficulty in overcoming the presumption against him established by the prosecution.

So far as known, the appendix is simply a vestigial organ, absolutely without function but distinctly responsible for much morbidity and for many thousands of deaths annually. It would seem, therefore, to be almost criminal for an operator with the abdomen open before him to leave the appendix behind, particularly in young people, in any except the most unusual circumstances. Even with older patients the danger of subsequent appendicitis is not to be ignored. I recall one case of acute appendicitis with abscess formation in a man of 84, with recovery, and another at 76 but with extensive adjacent involvement and fatal issue.

On one occasion I accidentally entered the operating room of a colleague just as he had reopened the abdomen because of the advent of acute symptoms three or four days after his removal of an appendix, and there saw that the *encircled piece of cecal wall had sloughed out* with outpouring of fecal contents and early death. Shortly afterward I was told of a similar case in the same hospital, as found at autopsy.

The "blowing off" of the ligature has been mentioned by those who resort to the more complicated procedure, but such an occurrence is to me inconceivable and has certainly never appeared in any of the thousands of cases which have come under my personal supervision and cognizance.

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Injection of Ether into the Uterus

To the Editor.—On page 129 of the July, 1928 issue of this Journal in the Proceedings of the Chicago Gynecological Society there appears the report of a demonstration by Dr. J. B. De Lee entitled, "A means of rupturing the uterus by injection of ether." The means he used to demonstrate the dangers of injecting ether into the uterus does not conform with two well established laws of physics; namely, that the boiling point of a liquid varies directly with the pressure and that the volume of a gas at a given temperature varies inversely as the pressure.

The writer performed a simple experiment as follows: a 10 c.c. bottle was connected by means of a piece of glass tubing through a cork with a sphygmomanometer. Three c.c. of ether were introduced into the bottle, and the stopper was then tightly inserted and the bottle was placed in a water-bath, and the pressure exerted by the expansion of the ether was recorded. At 100° F. the maximum pressure exerted by the ether vapor was 194 mm. Hg. Increasing the temperature would increase the pressure but at each rise in temperature the pressure became constant for that temperature.

Transuterine insufflation of the uterine tubes is a frequent procedure and 200 mm. Hg. pressure is considered perfectly safe even in a closed system. Presumably a pregnant uterus is open at at least two points, cervix and one tube. It is therefore inconceivable that a gas which will exert a maximum of pressure of 194 mm. Hg. could do damage to the uterus. Even granting the presence of blood clots or folds of mucous membrane the pressure is still within safe limits.

As I read Dr. DeTarnowsky's article on producing abortion by injecting ether into the uterine cavity it did not seem to me that the expulsion of the fetus was due to the explosive force of the ether vapor, but that the ether acted as a uterine irritant which caused expulsion of the fetus. If the desire is to "blow" the fetus out of the uterus, T.N.T. would be much more efficient than ether.

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Books Received

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LES ARTHRITES GONOCOCCIQUES. Par Henri Mondor, professeur agregé a la Facultè de Médecine de Paris. Avec 121 figures. Masson et Cie, editeurs. Paris, 1928.

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